American Journal of Obstetrics and Gynecology

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D.

Editorial Comment

Anemia in Pregnancy

ALTHOUGH almost a full century has passed since Walter Channing of Boston first described anemia in pregnancy, prior to the last ten years the progress of knowledge was essentially limited to descriptive and nosologic studies of this condition. Investigators were, for the most part, so thoroughly imbued with the belief in a positive etiologic agent, a *materies morbi,* that an untold amount of time and energy was devoted to the search for the hypothetic toxin which, elaborated by the product of conception, resulted in the development of anemia. The introduction of liver therapy in pernicious anemia a decade ago by Minot ushered in a virtual renaissance of fruitful research in the field of hematology. The work of Whipple, Minot, Castle, and their various associates established in a quantitative way the relationship of food, digestion, and absorption to blood formation. It therefore became obvious that the best method of attacking the problem of anemia in pregnancy would be by the study of these factors in pregnant women.

Early observers had demonstrated that there were different types of anemia in pregnancy, many of them dependent on well-established causes for anemia, such as hemorrhage, sepsis, nephritis, and the like. Two distinct types, however, remained associated with no obvious cause. One of these was morphologically similar to addisonian pernicious anemia, the other to simple hypochromic anemia. In 1928 there was recorded the first successful treatment of a case of pernicious anemia of pregnancy with liver by Deschamps and Froyez. Two years later an unequivocal demonstration of the successful treatment of hypochromic anemia of pregnancy with iron in adequate dosage was published by Strauss. Following these reports many investigators have established beyond question that in the absence of complications, pernicious anemia of pregnancy may be relieved by liver therapy and hypochromic anemia of pregnancy by iron therapy, *provided that in each instance an adequate amount of liver or iron be employed.* It has been shown that the mere administration of *some liver* or *some iron* is not sufficient. Enough

must be given, and by the appropriate route, for the individual case. In this respect neither pernicious nor hypochromic anemia in pregnancy differs from similar types of anemia in the nonpregnant.

The nature of the deficiency state resulting in addisonian pernicious anemia has been somewhat elucidated. A substance, to be found in liver, kidney, brain, placenta, and perhaps other organs, is necessary for normal hematopoiesis in man. This substance is apparently elaborated through the interaction of an enzyme-like factor found in normal human gastric juice and a substance present in the average human dietary. It has been shown that the gastric factor is not any of the common ferments of gastric juice. The dietary factor is frequently associated with foods rich in the vitamin B complex, although not to be identified with any of the known purified components of this vitamin. Evidence has further been produced which suggests that disturbances of intestinal absorption may result in a virtual deficiency of the product of interaction of the gastric and food factors.

Studies of pernicious anemia of pregnancy by Strauss have shown that the condition may result from a temporary suppression of secretion of Castle's gastric factor, from a lack of the dietary factor or from a combination of these two. Although defective absorption has not been demonstrated to be etiologically related to pernicious anemia of pregnancy, it seems probable that this does play a rôle in some cases.

Simple hypochromic anemia in nonpregnant individuals has been shown to be associated with a deficiency of available iron. This deficiency may result from an inadequate intake of iron, from impaired absorption or from loss from the body. The high incidence of gastric anacidity in patients with hypochromic anemia has suggested that this or some associated gastrointestinal defect results in malabsorption of iron. Pregnant women with hypochromic anemia have been shown to have a high incidence of gastric anacidity; many have partaken, not only during pregnancy, but frequently over a period of years, of diets low in iron content. Further, attention has been directed to the obvious fact that all the blood-forming materials which enter into the fetal organism are derived from the mother. This is comparable, as far as the maternal body economy is concerned, to chronic blood loss.

Pernicious anemia is relatively rare in pregnancy in the temperate zone. When it occurs it may be controlled by liver therapy, preferably administered parenterally. Its prevention in many instances is to be achieved by the administration of a diet rich in foods containing the vitamin B complex such as meat and other proteins.

Moderate degrees of hypochromic anemia are common in pregnancy. There is reason to believe that an adequate dietary for the pregnant woman will eliminate many of these cases. However, proper food is frequently costly and dietary habits of a lifetime are altered with difficulty. Hence, it should be of great interest to all concerned with maternal wel-

fare to note that the daily administration of as little as 0.5 gm. (7½ gr.) of ferrous sulphate to women during the last four months of gestation has prevented the development of hypochromic anemia in a large series of cases in spite of the fact that most of these women partook of diets which were considered inadequate. One of every four women of a control, untreated group of pregnant women developed hypochromic anemia with less than 70 per cent hemoglobin.

The conclusions that may be drawn from the studies that have been outlined are of practical significance. Anemias occur in pregnancy, not as a result of mysterious hypothetic toxins but from the same types of mechanism as produce similar anemias in the nonpregnant. The treatment must thus be, not the termination of pregnancy, but the exhibition of the proper, *proved,* therapeutic agents. Hypochromic anemia in pregnancy is to be prevented by the use of some simple iron salt, in adequate amount, and the employment of diets containing adequate amounts of blood-building materials.

In Memoriam

WILLIAM BLAIR-BELL

IT IS with deep sorrow that we record the death, at the age of 65, on January 25, of Professor Blair-Bell, the distinguished English gynecologist, author, editor, and research worker. He was well known in this country and was made an honorary member of the American Gynecological Society in 1923 after having been its official guest speaker at the annual meeting in 1922. Professor Blair-Bell made numerous outstanding contributions to the literature of his specialty, but his chief efforts were devoted to two problems—the physiology of the ductless glands and the treatment of cancer by chemical agents. His American colleagues may well acknowledge Blair-Bell's genius, a man to whom they owe tribute for the monumental services which make his eventful career an outstanding one in Anglo-American medicine.

Society Transactions

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF OCTOBER 3, 1935

The following papers and discussion were presented:

The Incidence and Treatment of Secondary Anemia in Out-Patient Maternity Cases. Dr. O. J. Toland. (For original article, see page 640.)

Observations on the Use of Collip's Emmenin in the Menopause. Dr. Catharine Macfarlane. (For original article, see page 663.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 18, 1935

The following cases with discussions were presented:

Fatal Case of Yeast Meningitis in Pregnancy. Dr. H. J. Timerman. (For original article, see page 686.)

On Thyroid Rests. Dr. Otto Kampmeier.

A Normal Human Ovum in a Stage Preceding the Primitive Streak. Drs. E. A. Edwards, H. O. Jones and John I. Brewer. (For original article see page 672.)

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 4, 1935

The following case reports and papers were presented:

Primary Tuberculosis of the Vagina. Dr. J. L. McGoldrick. (For original article, see page 684.)

Adenocarcinoma of Supernumerary Breasts of the Labia Majora in a Case of Epidermoid Carcinoma of the Vulva. Dr. H. J. Greene. (For original article see page 660.)

Interstitial Radiation of the Cervix with a Suggested Modification of Taussig's Operation. Dr. C. Duncan. (For original article, see page 623.)

WASHINGTON GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 26, 1935

The following papers were presented:

An Analysis of 569 Forceps Operations. Dr. H. F. Kane and Dr. H. P. Parker. (For original article, see page 657.)

A New Breast Supporter for the Puerperium. Dr. B. Notes.

SPECIAL ARTICLE

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Survey of Obstetric and Gynecologic Opportunities in 89 Hospitals in the United States and 12 Hospitals in Canada, 1935

THE American Board of Obstetrics and Gynecology, as well as the other certifying boards for the various specialties, have recognized that certain fundamental training is necessary in the development of specialists in obstetrics and/or gynecology. The importance of graduate work in medicine is coming to be recognized by numerous agencies, including the Council on Medical Education of the A.M.A.

In 1932 the report on Obstetric Education of the White House Conference on Child Health and Protection was published. Consideration was given to graduate education and some quotations may be pertinent.

"Graduate work is quite different, having rather definite and well understood meaning in other fields of education. Most universities have graduate schools where advanced students can do intensive, specialized and original work which leads to the granting of an advanced degree. A few medical schools have undertaken to conduct a graduate school of this type, with the granting of a master's or a doctor of philosophy degree after two or three years of training. Other schools do real graduate work and offer fine opportunities without the establishment of a graduate school of medicine and without granting a degree. Whether or not a degree is granted does not seem to be essential, but there is a definite difference in the character of the opportunities offered and in the type of education and training required, and this constitutes the real difference between so-called postgraduate and graduate training and education."*

"It is essential that teachers, investigators and well qualified specialists be continually trained in obstetrics. This can be done best by serious graduate work, which would take anywhere from four to ten years after graduation. The termination of this period of education and training would, of course, not be final, and the man would naturally continue to learn and improve. The best type of physician never completes his education. He is always moving forward."†

Students are gradually demanding and securing longer courses of informal and formal education in their chosen fields of medicine, but those who have failed to secure this training often have difficulty in orienting themselves. Many recent graduates do not know where to seek these opportunities. The American Board of Obstetrics and Gynecology realized some of the difficulties which prospective applicants for certification encountered in meeting the following established requirements:

Group A. Those who have limited their practice to obstetrics and/or gynecology for a period of ten years or more, having had adequate special training.

Group B. Those who have had: (1) at least one year of interne service; (2) five years or more of practice thereafter, including at least three years of special training in obstetrics and/or gynecology satisfactory to the Board of Directors; (3) and who are now limiting their practice to obstetrics and/or gynecology.

*Obstetric Education Report of the Subcommittee on Obstetric Teaching and Education, p. 8. The Century Company, New York and London, 1932.

†Ibid, p. 10.

Therefore, it appointed from its members a committee consisting of Drs. E. D. Plass, J. C. Litzenberg, and F. L. Adair, Chairman. Under the direction of this committee, the following questionnaire was sent out to those hospitals which were approved for special training in obstetrics and/or gynecology by the Council on Medical Education and Hospitals of the A.M.A. There are certain limitations of this method of securing information but it seemed to be the only procedure available at the time.

Some of the hospitals appeared to be frankly puzzled as to the exact information which was desired and the replies were often irrelevant and difficult to interpret. This led to incompleteness in data which in some instances could be completed only from the Directory of the A.M.A. or from the "Annual Presentation of Educational Data" by the Council on Medical Education and Hospitals of the A.M.A. for the Session of 1934-1935. (J. A. M. A., August 31, 1935.)

A tabulated report of the information secured from the various hospitals is appended, which should prove of assistance to those who desire to secure additional experience and education in the field of obstetrics and gynecology and to the institutions which desire to secure the best possible type of professional men for their house staff.

The Board hopes that this report will stimulate many institutions to enlarge their house staff and to make residencies an integral part of their staff organization. The importance of graduate work must be more fully realized and steps taken by medical colleges to incorporate systematic graduate instruction in their scheme of medical education.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Office of Secretary

1015 Highland Building, Pittsburgh, (6) Pa.

In connection with the survey of graduate training facilities in obstetrics and gynecology in the United States and Canada being made by this Board, we lack certain data in those previously furnished by your hospital. Will you please fill out and return the enclosed blank at your earliest possible convenience. We desire to have all data as complete as possible so that they may be included in the publication now being prepared.

PAUL TITUS, M.D., *Secretary.*

Please specify regarding particular details.

Interneships (I)	Assistant Residencies (A.R.)
1. Length of service I.----------	A.R.----------
Begins I.----------	A.R.----------
2. No. of appointments I.----------	A.R.----------
Salary per month I.----------	A.R.----------
Maintenance I.----------	A.R.----------

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3. Previous interneship required I.---------- A.R.----------

Is Ob./Gyn. service combined or separated?----------

Are house officers limited to one service or do they rotate?

Who is the Chief of Service? Ob. ----------

Gyn. ----------

Residencies

Are appointments only by promotion?

Signed _____

Position _____

Hospital _____

City and State _____

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Office of Secretary

1015 Highland Building, Pittsburgh, (6) Pa.

This Board is now making a check of the material collected in the course of its survey of graduate training facilities in obstetrics and gynecology in the United States and Canada.

Will you please carefully look over the information given below for your Hospital, check it if accurate, correct it in the case of error, and fill in any missing portions. (We have used pencil in order to facilitate your corrections.) We are making an effort to get these data assembled and in pamphlet form by this Fall, and shall greatly appreciate your prompt return of this sheet.

PAUL TITUS, *Secretary.*

Hospital _____

Chief of Service _____

_____

_____

_____

*Diplomate, Am. Brd. Obst. & Gyn.

Candidates should apply to _____

Appointments made _____

LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND GYN. APPTS.	SALARY	MAINTENANCE	PREVIOUS INTERNESHIP	APPTS. ONLY BY PROMOTION?	COMMENT

No. of ob. & gyn. patients last year (estimated): Ob._____ Gyn._____

No. of beds: Obstetric_____ Gynecologic_____ Total_____

Signed _____

Position _____

Hospital _____

City and State _____

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Hillman Hospital, Birmingham, Ala.	*Obstetrics* Dr. F. A. Lupton Dr. J. G. Vance *Gynecology* Dr. S. G. Stubbins Dr. M. Y. Dabney	Director of the Hospital	Internes Dec. 1; Residents May 1	*Ob.* 2087 *Gyn.* 825	*Ob.* 50 *Gyn.* 38	Internes	1 yr.	July 1	3	None	Yes	No		Rotating service incl. 6 wk. Gyn., 3 wk. Ob.
						Residents	1 yr.	July 1	2	$ 30	Yes	1 yr.	Preferred	Rotating service incl. 6 mo. ea. Ob. and Gyn.
Los Angeles County Hospital, Los Angeles, Calif.	*Obstetrics* Dr. L. G. McNeile* *Gynecology* Dr. Wilburn Smith	Medical Director	Jan. and July	*Ob.* 6465 *Gyn.* 1611	*Ob.* 220 *Gyn.* 72	Internes	1 yr.	Varies		None	Yes	No		Rotating service incl. 6 wk. ea. Ob. and Gyn.
						Residents	3 yr.	July and Jan.	6	$ 10-$ 75	Yes	1 yr.	By Civil Service Exam.	First 18 mo. Ob., last 18 mo. Gyn.
White Memorial Hospital, Los Angeles, Calif.	Dr. R. J. Thompson	Medical Supt.	July 1	*Ob.* 1152 *Gyn.* 1000	*Ob.* 22 *Gyn.* 45	Internes	1 yr.	July 1	10g	$ 40	No	No		Rotating service incl. 10 wk. Ob., 5 wk. Gyn.
						Residents	3 yr.		2	$ 60-$112	No	Yes	No	Rotating betw. Ob. and Gyn. the 3 yr.
Children's Hospital, San Francisco, Calif.	Dr. H. A. Stephenson*	Medical Director	Before Mar. 1	*Ob.* 645	*Ob.* 44 *Gyn.* No record	Internes	1 yr.	July 1	8	None	Yes			Rotating service incl. 24 wk. Ob., 12 wk. Gyn.
						Asst. Res.	1 yr.	Aug. 1	8	$ 25	Yes	Yes	No	

San Francisco Hospital, San Francisco, Calif.	W. G. Moore* A. V. Pettit* K. L. Schaupp	Dean, U. of Calif., or Dean, Stanford U.		*Ob.* 1553 *Gyn.* 1013	*Ob.* 56 *Gyn.* 63	House Officer	1 yr.	July 1	1	$ 50	Yes			Rotating incl. 4 mo. Ob. and Gyn., rest Genl. and Ortho. Surg.
						Senior House Officer	1 yr.	July 1	2	$ 75	Yes			
Stanford University Hospital, San Francisco, Calif.	Dr. Ludwig Emge*	Director of the Hosp. or Chief of Staff	Dec. or Jan., closing Dec. 1	*Ob.* 619 *Gyn.* 685	*Ob.* 25 *Gyn.* 10[1]	Internes	1 yr.	July 1	3	None	Yes	No		
						Asst. Res.	1-2 yr.	July 1	2	$ 25-$ 50	Yes	Yes		
						Residents	1 yr.	July 1	1	$ 75	Yes	Yes	Yes	
University of California Hospital, San Francisco, Calif.	Dr. F. W. Lynch*	Dean's office, U. of Calif. Med. Center	February (Apply before Jan. 1)	*Ob.* 545 *Gyn.* 590	*Ob.* 24 *Gyn.* 29	Internes	1 yr.	June 1	3	None	Yes	No		Rotating service incl. 6 mo. ea. on Ob. and Gyn.
						Asst. Res.	2 yr.	July 1	2	$ 25-$ 50	Yes	Yes	No	6 mo. ea. Ob. and Gyn.
						Residents	1 yr.		1	$ 75	Yes	Yes	No	
Santa Clara County Hospital, San Jose, Calif.	Dr. A. A. Shufelt*	Dr. Doxey R. Wilson	Jan. 15	*Ob.* 741 *Gyn.* 349	*Ob.* 24 *Gyn.*[2]	Internes	1 yr.	July 1	9	$ 25	Yes			Rotating service incl. 6 wk. ea. Ob. and Gyn.
						Residents	1 yr.	July 1	3	$100	Yes	Yes	Yes	Ob. combined with Pediatrics
New Haven Hospital, New Haven, Conn.	Dr. A. H. Morse*			*Ob.* 436 plus OPD *Gyn.* 447	*Ob.* 20 *Gyn.* 26	Internes	20 mo.	March, July, Nov.	6	None	Yes	No		Rotating service incl. 8 wk. ea. Ob. and Gyn.
						Asst. Res.	6 mo.	July and Jan.	4	Yes	Yes	Yes	Yes	Combined Ob. and Gyn.
						Residents	1 yr.	July	1	Yes	Yes	Yes	Yes	Ranks as Jr. Instructor in Med. School

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Columbia Hospital for Women, Washington, D. C.	*Obstetrics* Dr. Prentiss Willson* Dr. W. M. Sprigg Dr. J. J. Mundell* Dr. Richard Silvester *Gynecology* Dr. E. W. Titus* Dr. G. B. Miller Dr. J. F. Crowley* Dr. T. J. Kelly	Supt. of Hospital	2 residents April or May; 2 more Oct. or Nov.	*Ob.* 1746 *Gyn.* 1351	*Ob.* 69 *Gyn.* 56	Residents	1 yr.	Jan. 1 and July 1	2 every 6 mo	None	Yes	Yes		Straight Ob./Gyn. service.
Gallinger Municipal Hospital, Washington, D. C.	Dr. H. F. Kane*	Supt. of Hospital	Jan. 1	*Ob.* 1721 *Gyn.* 1236	*Ob.* 106 *Gyn.* 80	Internes	1 yr.	July 1	24g	$ 15	Yes			Rotating service incl. 4 wk. ea. Ob. and Gyn.
						Residents	1 yr. minimum	July 1	2	$ 50	Yes	Yes	Yes	Rotation betw. Ob./Gyn.
Grady Hospital, Atlanta, Ga.	Dr. J. R. McCord*	Dr. McCord	Jan. 1	*Ob.* 3711 *Gyn.* 1147	*Ob.* 92 *Gyn.* 55	Internes	2 yr.	July 1	2	$ 15	Yes	No	Competitive	Rotating on Ob./Gyn.
						Asst. Res.	1 yr.	July 1	2	$ 25	Yes	Yes	Competitive	Rotating on Ob./Gyn.
						Residents	1 yr.	July 1	2	$ 50	Yes	Yes	Yes	

University Hospital, Augusta, Ga.	*Obstetrics* Dr. Joseph Akerman *Gynecology* Dr. W. H. Goodrich	Supt. of Hospital	Nov.	*Ob.* 1201 *Gyn.* 2851[3]	[4]	Internes	1 yr.	July 1	10	$ 10 with $5 bonus	Yes	No		Rotating service incl. 6 wk. ea. Ob. and Gyn.
						Asst. Res.	1 yr.	July 1	Ob. 1	$ 50	Yes	Yes	Yes	
						Residents	1 yr.	July 1	Ob. 1	$100	Yes	Yes	Yes	
Chicago Lying-In Hospital, Chicago, Ill.	Dr. F. L. Adair*	Dr. Adair	Internes: Jan., Apr., July and Oct. 1 Residents: Jan. and July 1	*Ob.* 3398 *Gyn.* 597	*Ob.* 150 *Gyn.* 12	Internes	9 mo.	Ob. qrtrly.; Gyn. Jan. & July 1	Ob. 20 Gyn. 2	None	Yes	Yes		Straight service
						Residents	3 yr.	Jan. and July 1	6	$33.33 to $75	Yes	Yes	Yes	
Chicago Maternity Center, Chicago, Ill.	*Obstetrics* Dr. J. B. DeLee*					Internes	1 yr.	Qrtrly.	10	$ 15	Yes	Yes		Rotating service incl. 3 mo. on Ob.
						Residents	1 yr.							
Cook County Hospital, Chicago, Ill.	*Obstetrics* Dr. D. S. Hillis *Gynecology* Dr. F. H. Falls*	Warden of the Hospital	Jan. 1 and July 1	*Ob.* 4200 *Gyn.* 2480	*Ob.* 200 *Gyn.* 100	Internes	18 mo.	Jan. 1 and July 1		None	Yes			Rotating service incl. some time on Ob. and Gyn.
						Residents	1 yr.	Jan. 1 and July 1	4	None	Yes	Yes	Preferred	
Passavant Memorial Hospital, Chicago, Ill.	Dr. A. H. Curtis*	Director of Internes		*Ob.* 551 *Gyn.* 503	*Ob.* 26 *Gyn.* 39	Internes	1 yr.							2 mo. ea. Ob. and Gyn.
						Residents	Ob. 6 mo. Gyn. 1 yr.	Ob. Jan. 1 and July 1 Gyn. July 1	Ob. 1 every 6 mo. Gyn. 1	None	Yes	Yes	No	

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Illinois Research and Educational Hospital, Chicago, Ill.	Dr. F. H. Falls*	Dr. Falls	Early in April	*Ob.* 750 plus OPD *Gyn.* 370	*Ob.* 27 *Gyn.* 13	Internes	18 mo.	July 1	3	None	Yes	No		Rotating; 6 or 15 wk. Ob.;[5] 6 wk. Gyn.
						Asst. Res.	1 yr.	July 1	1	$41.66	Yes	Yes	Usually	O.P. service 8 mo.; hospital service 4 mo.
						Residents	1 yr.	July 1	1	$83.33	Yes	Yes	Usually	Same as Asst. Res.
St. Luke's Hospital, Chicago, Ill.	Dr. H. O. Jones*	Office of the Director	Jan.	*Ob.* 948 *Gyn.* 694	*Ob.* 44 *Gyn.* Varies	Internes	1 yr.	Jan., Apr. and July 1	23g	None	Yes	No	Competitive exam.	Rotating service incl. 6 wk. ea. Gyn. and Ob.
						Residents	1 yr.	July 1	2	None	Yes	Yes	Yes	6 mo. Ob., 6 mo. Gyn.
Coleman (Indiana U.) Hospital, Indianapolis, Ind.	*Obstetrics* Dr. H. F. Beckman* *Gynecology* Dr. F. C. Walker*	Administrator of Hosp.	Jan.	*Ob.* 1153 *Gyn.* 811	*Ob.* 24 *Gyn.* 24	Internes	1 yr.	July 1	5	$12.50	Yes	No		Monthly rotation
						Residents	1 yr.	July 1	Ob. 1 Gyn. 1	$33.33	Yes	Yes	Yes	Gyn. resident spends 6 mo. Gyn., 6 mo. Surgery
University Hospitals, Iowa City, Ia.	Dr. E. D. Plass*	Supt. of Hosp., or Chief of Staff	Feb. 1	*Ob.* 1398 *Gyn.* 1214	*Ob.* 75 *Gyn.* 50	Senior Internes	1 yr.	July 1	3	$ 20	Yes	Yes	No	Rotating service
						Asst. Res.	1 yr.	July 1	1	$140	Yes	Yes	Usually	Appointment made by University
						Residents	1 yr.	July 1	1		Yes	Yes	Usually	

University of Kansas Hospital, Kansas City, Kan.	Dr. L. A. Calkins*	Dr. Calkins	Dec. 1	*Ob.* 1000 *Gyn.* 600	*Ob.* and *Gyn.* 42	Internes	1 yr.	July 1		$ 15	Yes	No		Rotating service incl. 6 wk. ea. Ob. and Gyn.
						Junior Residents	1 yr.	July 1	1	$ 50	Yes	Yes		
						Asst. Res.	1 yr.	July 1	1	$ 75	Partial	Yes		
						Residents	1 yr.	July 1	1	$100	Yes	Yes		
Charity Hospital, New Orleans, La.		Supt.	April, May or June	*Ob.* *Gyn.*	*Ob.* *Gyn.*	Internes								
						Junior Fellow	1 yr.	July 1	2	$ 25	Yes	2 yr. rotating		
						Senior Fellow	1 yr.	July 1	2	$ 50	Yes	Yes	Yes	
Touro Infirmary, New Orleans, La.	*Obstetrics* Dr. W. E. Levy* *Gynecology* Dr. C. J. Miller*		Early in Jan.	*Ob.* 996 *Gyn.* 1002	*Ob.* 41[6] *Gyn.* 66[6]	Internes	1 yr.	July 1		$ 10	Yes	No		
						Residents	1 yr.	July 1	2	$ 25	Yes	Yes	Preferred	Residents alternate in Gyn. & Ob. every 6 mo.
Johns Hopkins Hospital, Baltimore, Md.	*Obstetrics* Dr. J. McF. Bergland* *Gynecology* Dr. T. S. Cullen	Director of the Hospital	Jan. 1	*Ob.* 1708 *Gyn.* 1238	*Ob.* 58 *Gyn.* 46	Internes	1 yr.	Sept. 1	Ob. 5 Gyn. 4	None	Yes	No		Nonrotating service
						Asst. Res.	3 yr.	Sept. 1	Ob. 2 Gyn. 1	$ 20	Yes	Required	Yes	
						Residents	1 yr.	Sept. 1	Ob. 1 Gyn. 1			Required	Yes	
Mercy Hospital, Baltimore, Md.	*Obstetrics* Dr. C. E. Brack *Gynecology* Dr. Wm. Gardner	Board of Governors	Jan.	*Ob.* *Gyn.*	*Ob.* *Gyn.*	Internes	1 yr.	July 1	1	None	Yes	No		Genl. rotating
						Asst. Res.	1 yr.	July 1	1	$ 25	Yes	Yes		
						Residents	1 yr.		1	$ 50			Yes	

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
St. Joseph's Hospital, Baltimore, Md.	*Obstetrics* Dr. W. W. Gray *Gynecology* Dr. Leo Brady Dr. T. K. Galvin	Secy. of Executive Com.	Dec.	*Ob.* *Gyn.*	*Ob.* *Gyn.*	Internes	1 yr.	July 1		None	Yes			Rotating service
						Asst. Res.	1 yr.	July 1	1	None	Yes	Yes	Usually	Straight Ob.-Gyn. service
						Residents	1 yr.	July 1	1				Usually	Straight Ob.-Gyn. service
Mt. Sinai Hospital, Baltimore, Md.	*Obstetrics* Dr. M. W. Aaronson *Gynecology* Dr. Alfred Ullman	Supt.	Early in Jan.	*Ob.* 759 *Gyn.* 335	*Ob.* 33 *Gyn.*7	Internes	1 yr.	July 1	Ob. 2	None	Yes	Preferred		Gyn. combined with Surgery
						Second Year Internes	1 yr.	July 1	Ob. 2	None	Yes	Preferred		
						Residents	1 yr.	July 1	Ob. 1	$47.50	Yes		Yes	
University of Maryland Hospital, Baltimore Md.	Dr. L. H. Douglass*	Supt. of Hosp. or Prof. of Obst.	Jan.	*Ob.* 1200 *Gyn.* 400	*Ob.* 68 *Gyn.* 20	Internes	1 yr.	July 1	2	None	Yes	No		Rotating service incl. 8 wk. ea. Ob. and Gyn.
						Asst. Res.	1 yr.	July 1	2	None	Yes	Yes	No	
						Residents	1 yr.	July 1	1	$ 35	Yes	Yes	No	
West Baltimore General Hospital, Baltimore, Md.	Dr. A. C. Tievmeyer			*Ob.* 325 *Gyn.* 800	*Ob.* 24 *Gyn.* 40									Ob. and Gyn. residencies discontinued

Boston Lying-In Hospital, Boston, Mass.	*Obstetrics* Dr. F. C. Irving*	Supt. of Hospital	May and Nov.	*Ob.* 3140 *Gyn.*	*Ob.* plus *Gyn.* =150	Internes	6 mo.	Monthly	Ob. 12	None	Yes	2 yr. in genl. hosp.		Obstetrics only
						Asst. Res.	6 mo.	Jan. and July		$83.33	Yes	Grad. Boston Lying-In		
						Residents	6 mo.	Jan. and July		$125	Yes	Grad. Boston Lying-In		
University Hospital, Ann Arbor, Mich.	Dr. N. F. Miller*	Dr. Miller		*Ob.* 425 *Gyn.*[18]	*Ob.* 40 *Gyn.* 95	Internes	1 yr.	July 1	2	None	Yes			Rotating service incl. 4 wk. ea. Ob. and Gyn.
						Asst. Res.	1 yr.	July 1	2	$ 25	Yes	1 yr.	Usually	
						Instructors	2 yr.	July 1	2	$120	No	2 yr.	Usually	Instructor and Jr. Instructor appointed by Med. Sch.
City of Detroit Receiving Hospital, Detroit, Mich.	*Obstetrics* Dr. W. F. Seeley* *Gynecology* Dr. H. W. Yates	Supt. of Hospital		*Ob.* 1652 *Gyn.* 1609	*Ob.* 65 *Gyn.* 52	Internes								From affiliated hospitals
						Junior Resident	1 yr.	July 15	Gyn. 1	$83.33	Yes	Yes	Yes	Preceded by 1 yr. as Jr. Res. in Ob., Herman Kiefer Hosp.
						Residents	1 yr.	July 15	Gyn. 1	$125	Yes	Yes	Yes	Preceded by 1 yr. as Sr. Res. in Ob., Herman Kiefer Hosp.

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Grace Hospital, Detroit, Mich.	*Obstetrics* Dr. M. A. Darling *Gynecology* Dr. Bruce Anderson	Director of Hospital	Dec. to Apr.	*Ob.* 869 *Gyn.* 883	*Ob.* plus *Gyn.*[8]	Internes	1 yr.	July 1 and Sept. 1	20-25g	$17.50 to $25.00	Yes	No		Rotating service incl. 9 wk. Ob., 4½ wk. Gyn.
						Resident		July 1	1	$37.50 to $50.00	Yes	Yes	Yes	
Harper Hospital, Detroit, Mich.	Dr. Geo. Kamperman*	Director of Hospital	Dec. and Jan.	*Ob.* 1105 *Gyn.* Not available	*Ob.* 100 *Gyn.*[7]	Junior Internes	1 yr.	July 1	Ob. 2 Gyn. 1	None	Yes	No	On recommend. Dean Med. Sch.	Rotating service incl. 8 wk. ea. Ob. and Gyn.
						Senior Internes	1 yr.	July 1	Ob. & Path. 1	$20.30	Yes	1 yr.	Yes	
						Asst. Res.	1 yr.	July 1	Ob. 1	$40.50	Yes	2 yr.	Yes	Straight Ob. service
						Residents	1 yr.	July 1	Gyn. 1	$81.00	Yes	3 yr.	Yes	Straight Gyn. service
Herman Kiefer Hospital, Detroit, Mich.	Dr. W. F. Seeley*	Chief of Service	July 1	*Ob.* 1981 *Gyn.* None	*Ob.* 65 *Gyn.* None	Internes								From affiliated hospitals, which are Seymour Hosp. (Eloise, Mich.), Receiving Hosp. (Detroit), and Med. Coll. of Wayne U. (Detroit, Mich.)
						Junior Residents	1 yr.	July 15	Ob. 1			Yes	Yes	
						Residents	1 yr.	July 15	Ob. 1			Yes	Yes	

Providence Hospital, Detroit, Mich.	Dr. A. K. Northrop	Supt. of Hospital	Jan. 1	*Ob.* 1895 *Gyn.* 272	*Ob.* 77 *Gyn.*[7]	Internes	1 yr.	July 1	17?	$ 20	Yes	No		Rotating service incl. 3 mo. Ob.
						Residents	1 yr.	July 1 Jan. 1		$100	Yes	1 yr.		
Woman's Hospital, Detroit, Mich.	*Obstetrics* Dr. L. E. Daniels *Gynecology* Dr. H. M. Nelson*	Supt. of Hospital	Latter part of Feb.	*Ob.* 1957 *Gyn.* 2049[9]	*Ob.* 100 *Gyn.* 120	Internes	1 yr.	July 1		$ 25	Yes	1 yr.		Rotating service incl. 5 mo. Ob.; 7 mo. Gyn., Surg., Med., Ped.
						Junior Resident	1 yr.	July 1		$ 75		2 yr.	Yes	
						Residents	1 yr.	July 1				3 yr.	Yes	
Minneapolis General Hospital, Minneapolis, Minn.	Dr. J. A. Urner	Dean, Grad. Sch., U. of Minn.; Dr. Urner; or Dr. J. C. Litzenberg	4-6 mo. before service begins	*Ob.* 1691 *Gyn.* 1111	*Ob.* 63 *Gyn.* 45	Internes	1 yr.							Rotating ea. month.
						Fellowships	3 yr.	July 1 and Jan. 1	2	$ 50-$ 75	$300 deducted for maint.	1 yr. req.	Yes	Fellows apptd. by Grad. Sch. U. of Minn.; leads to degree of Ph.D. in Ob./Gyn.
University of Minnesota Hospital, Minneapolis, Minn.	Dr. J. C. Litzenberg*	Chief of Service or Dean Grad. School	3 to 6 months before service begins	*Ob.* 476 *Gyn.* 831	*Ob.* 23 *Gyn.* 26	Internes	3-6 mo.	Qrtrly.	Ob. 1 Gyn. 1	None	Yes	1 yr. rotating		
						Junior Teaching Fellows	2 yr.	Jan. 1 and July 1	2	$ 50	$300 deducted for maint.	1 yr. req.	2nd yr., yes	Fellows appointed by Dean, Grad. Sch. U. of Minn.; leads to degree of Ph.D. in Ob./Gyn.
						Senior Teaching Fellows	1 yr.	Jan. 1 and July 1	2	$ 75	$300 deducted for maint.	2 yr. req.	Yes	

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Mayo Foundation Graduate School, Rochester, Minn.	Dr. R. D. Mussey*		Oct. 1 and Apr. 1	*Ob.* 420 *Gyn.* 500 plus	*Ob.* 28 *Gyn.*[4]	Fellow in Graduate School	3 yr.	Oct. 1 and Apr. 1	1 or 2 yrly.	$ 70	No	1 yr.	By selection	Fellow serves as asst. incl. approx. 1 yr. residency
Ancker Hospital, St. Paul, Minn.	*Obstetrics* Dr. A. G. Schulze* *Gynecology* Dr. L. W. Barry*	Supt. of Hospital	March	*Ob.* 1548 *Gyn.* 715	*Ob.* 50 *Gyn.* 25	Internes	1 yr.	July 1	None	None	Yes	No		
						Junior Teaching Fellows	2 yr.	Jan. 1 and July 1	1	$ 50		1 yr. req.	No	Fellows appointed by Dean, Grad. Sch. U. of Minn.; leads to degree of Ph.D. in Ob./Gyn.
						Senior Teaching Fellows	1 yr.	Jan. 1 and July 1	1			2 yr. req.	Yes	
Jewish Hospital, St. Louis, Mo.	Dr. F. J. Taussig*	Supt. of Hospital	Dec. 1	*Ob.* 420 *Gyn.* 438	*Ob.* 33 *Gyn.*[4]	Internes (Jr.)	1 yr.	July 1	10g	$ 15	Yes	No		Rotating service incl. 10 wk. ea. Ob. and Gyn.
						Internes (Sr.)	1 yr.	July 1	None	$ 40	Yes	1 yr.	Yes	
						Junior Residents	1 yr.	July 1	1	$ 60	Yes	1 yr. plus satisf. training	Yes	
						Residents	1 yr.	July 1	None	$ 80	Yes	2 yr.	Yes	

St. Louis City Hospital, St. Louis, Mo.	*Obstetrics* Dr. T. K. Brown Dr. T. Y. Ayars *Gynecology* Dr. T. K. Brown Dr. H. H. Helbing	Hospital Commissmissioner	Apr. 15 (Apply before Jan. 1)	*Ob.* 3882 *Gyn.* 1759	*Ob.* 60 *Gyn.* 62	Internes	1 yr.		24g	$ 25	Yes			Rotating service incl. 4 wk. ea. Ob. and Gyn.
						Asst. Res.	1 yr.	July 1	2	$ 75	Yes	Required	Yes	
						Residents	1 yr.	July 1	2	$100	Yes	Required	Yes	
St. Mary's Group of Hospitals, St. Louis, Mo.	Dr. Wm. H. Vogt*	Rev. Alphonse M. Schwitalla, S. J., Dean	May 1			Fellowships 1st year	1 yr.	July 1		$ 25				Upon successful completion of 3-yr. Fellowship, candidate receives degree of Master in Gyn. and Ob. fr. St. Louis Univ. School of Medicine Graduate School
						2nd year	1 yr.	July 1		$ 35			Yes	
						3rd year	1 yr.	July 1		$ 45			Yes	
Barnes & St. Louis Maternity Hospitals, St. Louis, Mo.	Dr. Otto H. Schwarz*	Chief of Service				Internes	1 yr.	July 1	7	None	Yes	1 yr.		10 mo. Ob., 2 mo. Gyn.
						Asst. Res.	1 yr.	July 1	2	$ 25	Yes		Yes	
						Residents	1 yr.	July 1	2				Yes	6 mo. ea. Ob. and Gyn.
Jersey City Medical Center, Jersey City, N. J.	*Obstetrics* Dr. S. A. Cosgrove* *Gynecology* Dr. Chas. Kelly Dr. Jos. Rector	Medical Director		*Ob.* *Gyn.*	*Ob.* *Gyn.* 70	Internes	1 yr.	July	Ob. 10 Gyn. 6	None	Yes	Yes		Rotating service incl. 3 mo. Ob., 2 mo. Gyn.
						Asst. Res.	½ yr.	Jan. and July	Ob. 4 Gyn. 1	None	Yes	2 yr. 6 mo. gyn.	Yes	
						Residents	½ yr. and 1 yr.	Jan. and July	Gyn. 2	None	Yes	2 yr. 6 mo. gyn.	Yes	

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Margaret Hague Maternity Hospital, Jersey City, N. J.	*Obstetrics* Dr. J. F. Norton* Dr. S. A. Cosgrove* Dr. E. G. Waters*	Medical Director	Quarterly	*Ob.* 5200 *Gyn.* None	*Ob.* 275 *Gyn.* None	Internes	1-3 mo.	First of each mo.	Ob. 13	None	Yes	No	Through affiliated hosps.	
						Residents	15 mo.	Qrtrly.	Ob. 5	Yes	Yes	Yes	No	
Albany Hospital, Albany, N. Y.	*Obstetrics* Dr. T. O. Gamble* *Gynecology* Dr. J. A. Sampson	Medical Director (Before Jan. 1)	Feb. 1	*Ob.* 771 *Gyn.* 1725	*Ob.* 36 *Gyn.* varies	Internes	1 yr.	July 1	16	None	Yes			8 spend 6 wk. on Ob.; 12 spend 6 wk. on Gyn.
						Residents	1 yr.	July 1	Ob. 1 Gyn. 1	$ 50	Yes	1 yr.	No	
Cumberland Hospital, Brooklyn, N. Y.	*Obstetrics* Dr. W. C. Meagher* *Gynecology* Dr. J. E. Jennings	Medical Supt.	Dec. and Jan.	*Ob.* 1274 *Gyn.* 450	*Ob.* 40 *Gyn.* 24	Internes	2 yr.	July 1		None	Yes	No		Rotating service; 2 mo. Ob. 1st yr., 4 mo. 2nd yr.
						Residents	1 yr.	July 1	Ob. 1	$100	Yes	2 yr.	Yes	Gyn. incl. with Surgery; Ob. incl. with Medicine
Jewish Hospital, Brooklyn, N. Y.	*Obstetrics* Dr. Joshua Ronsheim *Gynecology* Dr. L. S. Schwartz*	Professional Director	Dec., for 2nd ensuing year			Internes	6 mo.	Jan. 1 and July 1			Yes	1 yr.		
						Asst. Res.	6 mo.	Jan. 1 and July 1	Ob. 1		Yes	1 yr. and houseship	Yes	
						Residents	6 mo.	Jan. 1 and July 1	Ob. 1	$ 50			Yes	

King's County Hospital, Brooklyn, N. Y.	Dr. C. E. Rynd	Medical Supt.	May and Nov. for July and Jan. appts.	*Ob.* 2891 *Gyn.* 3113	*Ob.* 120 *Gyn.* 90	Internes								"No straight interneship offered"
						Asst. Res.	1 yr.	Jan. 1 and July 1	2	None	Yes	2 yr. rotating		6 mo. ea. on Ob. and Gyn.
						Residents	1 yr.	Jan. 1 and July 1	2	$100	Yes	Yes		
Long Island College Hospital, Brooklyn, N. Y.	Dr. A. C. Beck*	Chief of Service	Jan. 15	*Ob.* 1411 *Gyn.* 630	*Ob.* and *Gyn.* ab. 100	Internes	1 yr.	July 1	4	None	Yes	Yes		Rotating service incl. 6 mo. Ob., 6 mo. Gyn.
						Asst. Res.	1 yr.	July 1	2	$ 25	Yes		Yes	
						Residents	1 yr.	July 1	1	$ 50	Yes		Yes	
Methodist Episcopal Hospital, Brooklyn, N. Y.	Dr. O. P. Humpstone*	Senior Obstetrician		*Ob.*	*Ob.* 100	Internes	4 mo.		Ob. 2	None	Yes	Yes		No Gynecologic service
				Gyn.	*Gyn.*[4]	Asst. Res.	6 mo.	Jan. 1 and July 1	Ob. 1	None	Yes	2 yr. genl. hosp.	No	
						Residents	1 yr.		Ob. 1	$100			No	
Buffalo General Hospital, Buffalo, N. Y.	*Obstetrics* Dr. F. C. Goldsborough* Dr. W. T. Getman *Gynecology* Dr. F. C. Goldsborough* Dr. J. E. King*	Supt.	Dec. 15	*Ob.* 769 *Gyn.* 1012	*Ob.* 28 *Gyn.*[4]	Internes	1 yr.	July 1	1 every 3 mo.	None	Yes	No		Rotating service incl. 1 mo. Ob., 2 mo. Gyn.
						Asst. Res.	1 yr.	July 1	Ob. 1 Gyn. 1	$ 25	Yes	1 yr.	Usually	
						Residents	1 yr.	July 1	None	$ 50	Yes	2 yr.	Usually	
Bellevue Hospital, New York, N. Y.	Dr. W. E. Studdiford	Chief of Service	April 1	*Ob.* 1642 *Gyn.* 2242	*Ob.* 82 *Gyn.* 80	Internes	1 yr.	July 1	8	None	Yes	1 yr.		
						Residents	3 yr.	July 1	1	Yes	Yes	1 yr. genl.; 1 yr. Ob. & Gyn.	Yes	1st yr. Path. 2nd yr. Obst. 3rd yr. Gyn.

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Mt. Sinai Hospital, New York, N. Y.	*Attending Gynec.* Dr. R. T. Frank*	Director of Hospital		*Ob.* 5 *Gyn.* 600	*Ob.* None *Gyn.* 37	Internes	29 mo.	July 1			Yes	No	By examination	Rotating service incl. 1 mo. Gyn.—no Ob.
						Asst. Res.	6 mo.[12]	Feb. 1 and Aug. 1	Gyn. 2	$ 45	Yes	2 yr.		
						Residents	6 mo.[12]	Feb. 1 and Aug. 1	Gyn. 2	$ 45	Yes		Yes	
New York Hospital, New York, N. Y.	Dr. H. J. Stander*	Supt. (Before Jan. 1)	1st Tues. in Feb.	*Ob.* 3800 *Gyn.* 1200	*Ob.* 137 *Gyn.* 40	Junior Internes	1 yr.	July 1	10	None	Yes	1 yr.		Full time on Obstetrics
						Senior Internes	1 yr.	July 1	4	$ 25-$ 50	Yes	2 yr.	Yes	Rotation betw. Ob. and Gyn.
						2nd Asst. Resident	1 yr.	July 1	3	$ 25-$ 50	Yes	3 yr.	Yes	Rotation betw. Ob. and Gyn.
						1st Asst. Resident	1 yr.	July 1	2	$ 25-$ 50	Yes	4 yr.	Yes	Rotation betw. Ob. and Gyn.
						Residents	1 yr.	July 1	1	$100	Yes	5 yr.	Yes	In charge of both services
New York Nursery and Child's Hospital, New York, N. Y.														Private and semiprivate Ob. cases only; no ward cases
New York Post-Graduate Hospital, New York, N. Y.	*Gynecology* Dr. W. T. Dannreuther*	Supt. of Hospital		*Ob.* None *Gyn.* 338	*Ob.* None *Gyn.* 37	Internes	27 mo.	Qrtrly.		None	Yes	No		No obstetrics
						Residents	1 yr.	Oct. 1	Gyn. 1	$ 90	Yes	2 yr.	Preferred	

Sloane Hospital for Women, New York, N. Y.	Dr. B. P. Watson*	Exec. Vice-Pres.	Every 2 mo.	*Ob.* 2287 *Gyn.* 787	*Ob.* 108 *Gyn.* 40	Internes	1 yr.	Every 2 mo.	6	None	Yes	1 yr.		Rotating service incl. 6 mo. Ob., 2 mo. Gyn.
						Asst. Res.	2 yr.	July 1	2	$ 50-$ 75	Yes	2 yr.	Yes	Rotating service incl. 4 mo. ea. Ob. and Gyn. clinic
						Residents	1 yr.	July 1	1	$125	Yes	2 yr.	Yes	
Woman's Hospital in the State of New York, New York, N. Y.	*Obstetrics* Dr. G. G. Ward* Dr. A. H. Aldridge* Dr. R. A. Hurd* *Gynecology* Dr. G. G. Ward* Dr. E. A. Bullard* Dr. R. M. Rawls* Dr. L. K. P. Farrar* Dr. R. A. Hurd* Dr. A. H. Aldridge*	Dr. Ward, Chief Surgeon	Six mo. in advance	*Ob.* 1591 *Gyn.* 1976	*Ob.* 89 *Gyn.* 130	Residents	2 yr.	Qrtrly.	8	None ($50 bonus)	Yes	1 yr.	Yes	Resident service divided into 1½ yr. Gyn., ½ yr. Ob.
						Chief Resident Gynecologist	1 yr. or longer	July 1	Gyn. 1	118.75		1 yr.	Yes	
Rochester General Hospital, Rochester, N. Y.	*Obstetrics* Dr. J. K. Quigley* *Gynecology* Dr. H. L. Prince	Chief Resident Physician	Apr. 1	*Ob.* *Gyn.*	*Ob.* *Gyn.*	Internes	1 yr.	July 1	8	$ 15	Yes	No		Rotating interneship. Gyn. service part of Surg.
						Asst. Res.	1 yr.	July 1	4	$ 25	Yes	Yes	No	
						Residents							No	
Strong Memorial Hospital, Rochester, N. Y.	Dr. K. M. Wilson*	Chief of Staff or Director of Hosp.	Jan. 1	*Ob.* *Gyn.* 8181[11]	*Ob.* *Gyn.* 291[11]	Internes	1 yr.	July 1	5	None	Yes	No		
						Asst. Res.	1 yr.	July 1	3	$41.66	Yes	Yes	No	No rotating service
						Residents	1 yr.	July 1	1	$83.33	Yes	Yes	Yes	

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNSHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Duke Hospital, Durham, N. C.	Dr. B. F. Carter Dr. R. A. Ross* Dr. E. C. Hamblen*	Supt. of Hospital	Dec.	*Ob.* 429 *Gyn.* 789	*Ob.* *Gyn.* 106	Internes	1-2 yr.	July 1	3	None	Yes	1 yr.		Rotating service
						Asst. Res.	3 yr.	July 1	3	$ 40	Yes		Yes	
						Residents		July 1	1	$ 80	Yes		Yes	
Cincinnati General Hospital, Cincinnati, Ohio	*Obstetrics* Dr. H. L. Woodward *Gynecology* Dr. F. Coppock		Feb. or March	*Ob.* 2284 *Gyn.* 1135	*Ob.* 60 *Gyn.* 60	Internes	1 yr.	July 1		None	Yes	No		Rotating interneship with 1 mo. Ob.[13]
						Asst. Res.	1 yr.	July 1	Ob. 1	$41.65	Yes	Yes	No	Asst. Res. in Surg. has 6 mo. Gyn.
						Residents	1 yr.	July 1	Ob. 1	$ 50	Yes	Yes	No	
Mt. Sinai Hospital, Cleveland, Ohio	*Obstetrics* Dr. M. Garber *Gynecology* Dr. J. L. Dubis	Director of Hosp.	Dec.	*Ob.* IP 600 OP 250	*Ob.* 45	Internes	1 yr.	July 1	Ob. 1 Gyn. 1	$ 10	Yes		No	
				Gyn. IP 799 OP 613	*Gyn.* varies	Residents	1 yr.	June 30	Ob. 1	$ 60	Yes	Yes	Usually	
St. Ann's Hospital, Cleveland, Ohio	Dr. E. P. Monaghan	Secy. of Staff	Feb.	*Ob.* 1500 *Gyn.* None	*Ob.* 75 *Gyn.* None	Internes			2	None	Yes	No		Rotate fr. St. Alexis and Charity Hosps. for Ob.
						Residents	1 yr.	July 1	2	$ 50	Yes	Yes	Yes	Very little Gyn.

St. John's Hospital, Cleveland, Ohio	*Obstetrics* Dr. C. A. O'Connell *Surgery incl. Gynec.* Dr. G. P. O'Malley	Interne Committee or Sister M. Carmelita	Middle of Dec.	*Ob.* 615 *Gyn.* 238	*Ob.* 28	Internes	1 yr.	July 1	6	$12.50	Yes	No		Rotating, Gyn. incl. with Surgery
						Junior Residents	1 yr.	July 1	Ob. 1	$ 25	Yes	Yes		
						Resident	1 yr.	July 1	Ob. 1	$ 50	Yes	Yes		
St. Luke's Hospital, Cleveland, Ohio	*Obstetrics* Dr. A. J. Skeel	Supt. of Hospital	Dec. 1-10	*Ob.* 1013 *Gyn.* 264	*Ob.* 55 *Gyn.* varies	Internes	1 yr.	July 1	14g	None	Yes	No		Rotating
						Asst. Res.	1 yr.	July 1	Ob. 1	$ 25	Yes	Yes	Usually	
						Residents	1 yr.	July 1	Ob. 1	$ 75	Yes	Yes	Yes	
University Hospitals of Cleveland, Cleveland, Ohio	*Obstetrics* Dr. A. H. Bill* *Gynecology* Dr. A. H. Bill* Dr. W. H. Weir*	Director of Hosp.	Jan. 1	*Ob.* 2003 *Gyn.* 1188	*Ob.* 234 *Gyn.* 20	Asst. Res.	1 yr.	July 1	Ob. 4 Gyn. 2			Yes		No interneships
						Residents	1 yr.	July 1	Ob. 1 Gyn. 1				Usually	
Starling-Loving Hospital, Columbus, Ohio	*Obstetrics* Dr. Andrews Rogers* *Gynecology* Dr. Fred Fletcher* Dr. P. J. Reel	Interne Committee	Middle of Dec.	*Ob.* 634 *Gyn.* 368	*Ob.* 39[6] *Gyn.* 23[6]	Internes	1 yr.	July 1			Yes			Rotating service incl. 1½ mo. ea. on Ob. and Gyn.
						Residents	1 yr.	July 1	1	$ 75	Yes	Plus 2 yr. surg. res.		
Miami Valley Hospital, Dayton, Ohio	*Obstetrics* Dr. Gordon Erbaugh	Supt. of Hospital	Dec.	*Ob.* 881[14] *Gyn.* None	*Ob.* 44 *Gyn.* None	Internes	1 yr.	July 1	Ob. 1	$ 25	Yes	No		Rotating service with 1½ mo. Ob.; no Gyn.
						Residents	1 yr.	July 1	Ob. 1	$ 75	Yes	Yes	Usually	
Women's and Children's Hospital, Toledo, Ohio	Dr. W. W. Brand	Director of Hosp.	Jan. 1	*Ob.* 330 *Gyn.* 114	*Ob.* 50 *Gyn.*[10]	"Mixed Residency"	1 yr.	July 1		$ 25	Yes	Yes		Rotating residency incl. Ob., Med., Surg., Pediat.

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Hospital of Univ. of Ore. Med. Sch., Portland, Ore.	Dr. R. E. Watkins*	Dean of Univ.	Jan. 1	*Ob.* 701 *Gyn.* 993	*Ob.* 30 *Gyn.* 50	Residents	3 yr.	July 1	1	$ 30 $ 45 $ 55	Yes	Yes	No	Gyn. and Ob. combined
Multnomah Hospital, Portland, Ore.	Dr. R. E. Watkins*	Director of Hosp.	Internes: Dec. 1	*Ob.* *Gyn.*	*Ob.* *Gyn.*	Internes	1 yr.	July 1	16g	$ 20	Yes			Rotating, 2 mo. Ob. included
						Residents	1 yr.	July 1	3	$ 35	Yes	Yes		
Graduate Hospital, Philadelphia, Pa.	Dr. W. R. Nicholson* Dr. B. C. Hirst	Grad. Sch. of Med.	Feb. 15	*Ob.* 9[15] *Gyn.* 309	*Ob.* None *Gyn.* 40	Internes	2 yr.	July 1	8g	None	Yes	No		Rotating; 6 wk. Gyn. here; to Univ. Hosp. for 6 wk. Ob.
						Residents	1 yr.	July 1	Gyn. 1					Appointees must complete course in Ob. and Gyn. Grad. Sch., U. of Pa.
Hospital of the Univ. of Pa., Philadelphia, Pa.	*Obstetrics* Dr. C. C. Norris* *Gynecology* Dr. F. E. Keene*	Chief of Service (betw. Jan. and May)	May 1	*Ob.* 921 *Gyn.* 1123	*Ob.* 45 *Gyn.* 35[16]	Internes	2 yr.	July 1		None	Yes	No		Rotating service incl. 2 mo. Ob. and Gyn.
						Residents	1 yr.	Sept. 1	Ob. 1 Gyn. 1	None	Yes	Yes		

Kensington Hospital for Women, Philadelphia, Pa.	Dr. E. A. Schumann*	Chief of Service	Jan. 1 & July 1	*Ob.* 1107 *Gyn.* 484	*Ob.* 65 *Gyn.* 36	Junior Residents	6 mo.	Jan. 1 and July 1	Ob. 1	None	Yes	Yes		
						Residents	2 yr.	July 1	1	$ 25-$ 50	Yes	Yes	Yes	Rotating service incl. 12 mo. ea. Ob. and Gyn.
Pennsylvania Hospital, Philadelphia, Pa.	*Service "A"* Dr. C. B. Lull *Service "B"* Dr. R. A. Kimbrough, Jr.	Supt. or Chief of Service	Internes: apply by Nov. for Feb. appt.; Residents apply 2-3 mo. before start of service	*Ob.* 2565 *Gyn.* 649	*Ob.* 125 *Gyn.* 25	Internes	2 yr.	July 1	9	None	Yes			Rotating service incl. 81 days Ob. and Gyn.
						Residents	1 yr.	Jan. 1 and July 1	2	None	Yes	Yes	No	
Philadelphia General Hospital, Philadelphia, Pa.	Dr. F. C. Hammond* Dr. J. A. McGlinn Dr. E. A. Schumann* Dr. C. B. Lull Dr. C. Macfarlane* Dr. P. E. Williams* Dr. W. J. Thudium	Supt. of Hospital	June 1	*Ob.* *Gyn.*	*Ob.* *Gyn.*	Internes	2 yr.	July 1	60g	None	Yes	No		Rotating service with 2 mo. Ob.
						Asst. Res.	1 yr.	July 1	1	$100	Yes	Yes	Preferably	
						Residents							No	

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Elizabeth Steel Magee Hospital, Pittsburgh, Pa.	*Obstetrics* Dr. C. J. Barone Dr. B. Martinez Dr. Paul Dodds Dr. C. W. Ziegler *Gynecology* Dr. R. R. Huggins Dr. S. A. Chalfant* Dr. B. Z. Cashman	Supt. of Hospital	March or April	*Ob.* 2958 *Gyn.* 961	*Ob.* 136 *Gyn.* 65	Internes	1 yr.	July 1	18	None	Yes	No		Rotating service, incl. 60 days Ob., 40 days Gyn.
						Residents	1 yr.	Aug. 1	6	$41.66	Yes	Yes	Usually	
Memphis General Hospital, Memphis, Tenn.	*Obstetrics* Dr. W. T. Price* *Gynecology* Dr. W. T. Black*	Internes: to Interne Committee. Residents: to Chief of Service		*Ob.* 1869 *Gyn.* 859	*Ob.* 70 *Gyn.* 40	Internes	18 mo.	10th ea. month	1 ea. mo	$ 20	Yes	No	By class standing	Rotating service incl. 2 mo. Ob., 1 mo. Gyn.
						Residents	1 yr.	July 1	Ob. 1 Gyn. 1	$ 65	Yes	Yes	No	
Vanderbilt University Hospital, Nashville, Tenn.	Dr. L. E. Burch*	Chief of Service	Apr. 1	*Ob.* 359 *Gyn.* 392	*Ob.* 11 *Gyn.* 11	Internes	1 yr.	July 1	2	$23.75	Yes	Yes		Ob. and Gyn. combined
						Asst. Res.	2 yr.	July 1	2	$35.41	Yes	Yes	Usually	
						Residents	1 yr.	July 1	1	$75.00	Yes	Yes	Usually	

Baylor University Hospital, Dallas, Tex.	*Obstetrics* Dr. C. R. Hannah* *Gynecology* Dr. Elbert Dunlap	Medical Director (Before Mar. 15)	Apr. 1	*Ob.* 1033 *Gyn.* 1110	*Ob.* 50 *Gyn.* 75	Internes	2 mo.	1st of ea. mo.		$ 25	Yes	No		Rotating service incl. 2 mo. ea. Ob. and Gyn.
						Residents	1 yr.	July 1	Ob. 1 Surg. and Gyn. 1	$ 75	Yes	Yes	Yes	
Hospital of Medical College of Virginia, Richmond, Va.	*Obstetrics* Dr. H. H. Ware *Gynecology* Dr. I. A. Bigger	Supt. of Hospital Division		*Ob.* 900 *Gyn.* 1200	*Ob.* 31 *Gyn.*[7]	Internes	1 yr.		20	None	Yes	No		Rotating service with 3 mo. ea. Ob. and Gyn.
						Asst. Res.				$ 25				
						Resident	1 yr.		1	$ 50	Yes	Yes	No	
University of Virginia Hospital, University, Va.	*Ob. and Gynec.* Dr. T. J. Williams* *Surgery and Gynec.* Dr. E. P. Lehman	Supt. of Hospital	First week in Dec.	*Ob.* 500 *Gyn.* 400	*Ob.* 25 *Gyn.* 20[17]	Internes	1 yr.	July 1	6	None	Yes	No		Rotating with 2 mo. Ob. and Gyn.; 6 mo. Surg. and Gyn.
						Asst. Res.	1 yr.	July 1	1	None	Yes	Yes	Usually	
						Residents	1 yr.	July 1	1	$ 50	Yes	Yes	Usually	
State of Wisconsin General Hospital, Madison, Wis.	Dr. J. W. Harris*	Supt. of Hospital	July 1	*Ob.* 154 *Gyn.* 1200	*Ob.* 15 *Gyn.* 30	Internes	1 yr.	July 1	16g	None	Yes	No		Rotating interneship with 1 mo. on Ob. and Gyn.
						Asst. Res.	1 yr.	July 1	1	$ 50	Yes	Yes	No	
						Residents	1 yr.	July 1	1	$ 75	Yes	Yes	Yes	
Milwaukee County General Hospital, Wauwatosa, Wis.		Milwaukee County Civil Service		*Ob.* 1691 *Gyn.* 1065	*Ob.* 66 *Gyn.* 82	Internes (Jr.)	1 yr.	June 15	39g	$ 10	Yes	No		Rotating interneship
						Internes (Sr.)	1 yr.	July 1	19g	$ 50	Yes	Yes	Yes	
						Junior Physicians	1 yr.	July 15	2	$100	Yes	Yes	Yes	Appointment through Civil Service examination

CANADA

The data used below were obtained from a booklet entitled "*Summary of Senior Interneships and Residencies in Specialties in Canadian Hospitals,*" published by the Department of Hospital Service, Canadian Medical Association, and revised in 1935. For information as to first year Interneships at these hospitals, candidates are referred to the booklet entitled "*Hospitals in Canada Which Are Approved for Interneships,*" published by the same Department. No attempt has been made by the American Board of Obstetrics and Gynecology to give its "approval" to the various appointments listed below.

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNESHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
St. John General Hospital, St. John, New Brunswick						Junior Appt.	2 yr.			$ 25	Yes			Rotating, 13 wk. Ob., 13 wk. Surg., etc.
						Senior Appt.	1 yr.		None	$ 50				
Montreal General Hospital, Montreal, Quebec		General Supt.	Dec.		Total beds 600	Senior Appt.	1 yr.	July 1	Gyn. 1	None	Yes	1 yr. rotating req.		
Royal Victoria Hospital, Montreal, Quebec		Supt. of Hospital (Before Dec. 15)	End of year		Total beds 700	Senior Appt.	1 yr.	July 1	1	$ 80	Yes	Yes		Teaching hosp., McGill Univ. Nonrotating serve

Toronto General Hospital, Toronto, Ont.		Asst. Supt.	April or May		*Ob.* *Gyn.* 105	Senior Appt.	2 yr.		2	None	Yes	1 yr. req.		Teaching hosp. U. of Toronto. Total beds 552
St. Michael's Hospital, Toronto, Ont.		Dr. N. D'Arcy Frawley	Jan.		*Ob.* *Gyn.* 100	Senior Appt.	1 yr.	July 1	Ob. 1 Gyn. 1	None	Yes	Req.		Teaching hosp. U. of Toronto
Toronto Western Hospital, Toronto, Ont.		Supt. of Hospital	Jan.		Total beds 312	Senior Appt.	1 yr.	July 1	1	$ 50	Yes	1 yr. req.		Teaching hosp. U. of Toronto.
Victoria Hospital, London, Ont.		Supt. of Hospital	Dec.		Total beds 400	Senior Appt. (Resident)	1 yr.	July 1	1	$ 40	Yes	1 yr. req.	Preferred	Teaching hosp. U. of Western Ontario
Winnipeg General Hospital, Winnipeg, Man.		Supt. of Hospital	Jan. or early Feb.		*Ob.* *Gyn.* 100	Residents		July 1	2	$ 25-$ 50[19]	Yes	2 yr. req.		Total beds 663
St. Boniface Hospital, St. Boniface, Man.		*Gynecology* Dr. C. R. Rice			Total beds 471	Senior Appt.		June 1	Ob. 1 Surg. Gyn. 1		Yes	1 yr. req.	Preferred	Teaching hosp. U. of Manitoba
Royal Alexandra Hospital, Edmonton, Alta.		Supt. of Hospital	Feb. 1		Total beds 450	Senior Residents		July 1	3	$ 50	Yes	1 yr. req.		Service incl. 4 mo. Med., 8 mo. Surg. and Gyn.
University of Alberta Hospital, Edmonton, Alta.		Supt. of Hospital	Jan.		Total beds 354	Senior Internes	1 yr.	July 1	3	$ 50	Yes	Yes		Rotating, 4 mo. Gyn., G. U. and Ob., rest of time Surg. and Orthopaed. Teaching hosp. of U. of Alberta

HOSPITALS, ADDRESSES	CHIEF OF SERVICE	APPLY TO	APPOINTMENTS MADE	NO. OF PTS.	NO. OF BEDS		LENGTH SERVICE	SERVICE BEGINS	NO. OF OB. AND G. APPTS.	SALARY PER MO.	MAINTENANCE	PREVIOUS INTERNSHIP	APPOINTMENT ONLY BY PROMOTION ?	COMMENT
Vancouver General Hospital, Vancouver, B. C.		Secretary, Interne Committee	Dec.		*Ob.* 111	Senior Appts.	1 yr.	July 1	1	$100 less 10%	Yes	Yes		Total beds 1,037
St. Joseph's, Baltimore, Md.	Dr. W. W. Gray Dr. Leo Brady Dr. E. Harrison Dr. T. K. Galvin	Secretary Executive Committee	Dec.	*Ob.* 612 *Gyn.* 402	*Ob.* 33 *Gyn.* 30		1 yr.	July 1	2	None	Yes	Yes	Usually	Rotating service.

*Diplomate, American Board of Obstetrics and Gynecology.

g, In the column giving "No. of Ob. & Gyn. Appts.", small letter "g" means the total number of general rotating internes was given, rather than the number specifically reserved for obstetrics/gynecology. In many cases the figure supplied to us by the Hospital seemed too large to be the number of internes reserved for this specialty; in other instances the hospitals stated on the questionnaire that the figure given us was general rather than specific.

NB, Newborn. IP, Inpatient. OP, Out-patient.

[1]Additional private beds available. [2]Included in medical.

[3]2,851 patients admitted on Surgery, approximately one half being gynecologic patients. Beginning July 1, 1935, gynecologic patients to be admitted under that heading, not included under Surgery as previously.

[4]Beds or patients not segregated.

[5]The three months obstetric service in out-patient department is available only to half the total number of internes.

[6]Part clinic, part private. [7]Included in general surgery.

[8]No limit. Obstetrics=1 service of 29 rooms; ward service of 8 and 12 beds each.

[9]Including all adult surgery; gynecology not kept separate. [10]50 beds for medical and surgical patients.

[11]Plus Rochester Municipal Hospital obstetric and gynecologic patients totalling 2,088 and beds totalling 60.

[12]Subject to renewal. [13]And 12 internes have one month on Gynecology.

[14]Living births; number of obstetric patients not specific. [15]Nine emergency or operative cases last year.

[16]Including 31 ward beds, 4 semiprivate beds. Private gynecology beds can be supplied as required.

[17]This figure does not include gynecologic beds in department of Surgery and Gynecology.

[18]Gynecologic patients number 900 hospital cases, 8,400 out-patient department.

[19]Less such percentage deductions as may be in force from time to time.*

The following hospitals did not respond to re-check questionnaire sent out by this Board. Therefore, the data obtained and used from the following hospitals at the time this survey went to press may not be up to date: Chicago Maternity Center (Chicago); Charity Hospital (New Orleans); Mercy Hospital (Baltimore); St. Mary's Group of Hospitals (St. Louis); Barnes and St. Louis Maternity Hospitals (St. Louis); Jewish Hospital (Brooklyn, N. Y.); New York Nursery and Child's Hospital (New York City); Rochester General Hospital (Rochester, N. Y.); Multnomah Hospital (Portland, Ore.); Philadelphia General Hospital (Philadelphia).

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Physiology and Pathology of Pregnancy

Fairbairn, John S.: Are We Satisfied With the Results of Ante-Natal Care? Brit. M. J. 2: 193, 1934.

The author reviews antenatal work to determine where the weakness lies. The first duty is promoting normal physiologic function throughout the reproductive period, second, the correction of deviations from the normal function, and third, the *early* discovery of disordered function.

In the eagerness to search for pathology, obstetricians are leaving constructive physiologic hygiene too far in the background. Abortion and induced premature labor for hypothetical trouble has been overdone. There seems to be too little attention paid to the individual patient; she is studied more for her chemical and biochemical reactions than her mental responses. The author stresses the recent literature on the importance of the psychic factor during pregnancy and labor. Early disorders, such as slight losses of blood, vomiting that is not helped by simple remedies, mild albuminurias, and slight rise in blood pressure are not observed any closer than in the so-called normal patient, and these soon become complicated cases.

Lack of coordination and cooperation is noted between the antenatal clinics and the lying-in hospitals where the patient is delivered. The mother is taken care of by one member of the staff for prenatal, another for the intranatal, a third for the postnatal care of the mother, and another for the mother and infant in the infant welfare clinic. In this respect the family practitioner is the ideal supervisor throughout reproduction.

F. L. ADAIR AND I. BROWN.

Browne, F. J.: Are We Satisfied With the Results of Ante-Natal Care? Brit. M. J. 2: 194, 1934.

The author shows that nothing has been done to prevent malformations and stillbirths. In 1927 the stillbirth rate was 38 per 1,000 and in 1932 was 41 per 1,000. The death rate from eclampsia has changed little in the last twelve years. He suggests that eclampsia be a reportable disease to determine its geographic distribution. One explanation would be the decrease in birth rate, since the proportion of first births has increased steadily in the last twenty years over subsequent births, and eclampsia, accidental hemorrhages and difficult labors are more common in primiparas. The success of a prenatal clinic should be based mainly on the reduction of mortality and not on the number of registered patients. Usually examinations are too infrequent and unskilled. Midwives are given calipers for measurements, but yet no manometers which are even more necessary.

Operations are not always safe and operative interference is not always necessary. In the last published reports eight teaching hospitals in this country record forty-four deaths among their own booked cases, and of these twelve (27 per cent) followed cesarean section in originally "clean" cases, with most of the deaths due to general peritonitis. Self-criticism may be a help in the advancement toward mortality reduction.

F. L. ADAIR AND I. BROWN.

Cassie, Ethel: Are We Satisfied With the Results of Ante-Natal Care? Brit. M. J. 2: 197, 1934.

Antenatal care is not kept up to the minimum standards due not only to the faults of administration or faults in doctors or midwives but also to the women themselves. The average attendance per patient was 3 prenatal visits; and as there are many who make 5 to 8 visits, there must be some who make only one. Fifty-seven out of 87 patients with intercurrent disease showed inadequate prenatal care. In 64 of the 68 toxemias there was not enough prenatal care and in some none at all. The author suggests raising the health standard of the nation and also careful medical supervision during pregnancy.

Inadequate training of medical students and midwives is a factor. Often teachers are too few and are frequently overworked. However, antenatal work is "progressing as well as can be expected."

F. L. ADAIR AND I. BROWN.

Buchan, George F.: Are We Satisfied With the Results of Ante-Natal Care? Brit. M. J. 2: 199, 1934.

Objectives of antenatal care are as follows: (1) Maintaining the health of the pregnant woman, (2) delivery with the least disturbance to the woman, (3) birth of a healthy, full-term child, and (4) an adequate supply of breast milk for the child during lactation.

The health visitor should check on home conditions as well as on the cause of nonattendance to the prenatal clinic. (1) The prenatal health officer must be able to advise concerning the hygiene of pregnancy as well as the medical examination; (2) he should make inquiry into failures in keeping appointments; (3) the obstetrician making prenatal examinations should be in charge of the confinement and have sufficient experience to cope with any abnormality whether foreseen or not; and, (4) hospital beds should be available to those needing such accommodations.

Records must be kept by the physicians of all the important details of the individual case.

F. L. ADAIR AND I. BROWN.

Reiprich, W.: A New Rapid Pregnancy Test for Urine, Wien. klin. Wchnschr. **12:** 1441, 1933.

The author describes a new and rapid urine test for pregnancy. He uses immature rats in which large amounts of urine (10 to 25 c.c.) can safely be injected. When positive, the reaction is definitely present in twenty-four to thirty hours and can be determined macroscopically. A positive reaction is evidenced by marked hyperemia and a hypertrophy of the ovary (3 or 4 times that of the control animals). Rats are apparently more sensitive to the hormone than are mice. They also respond more rapidly.

RALPH A. REIS.

Dowell, D. M.: Preliminary Observations on the Menstrual Cycle and Pregnancy With a Simple Pregnancy Diagnostic Test, J. Missouri State M. A. **30:** 275, 1933.

The author injected a few minims of an extract of the anterior pituitary gland intradermally into the flexor surface of the forearms of pregnant and nonpregnant women. In the former group there was only a small intradermal wheal signifying a negative reaction and pregnancy. In the nonpregnant group the result obtained was a very marked degree of erythema about the wheal at the injected site, signifying absence of pregnancy. Whether this supposed test is due to an allergic reaction or not is merely a conjecture. This test has been accurate in the author's hands; it is simple, safe, and quite inexpensive.

J. THORNWELL WITHERSPOON.

Valle, Guiseppi: The Diagnostic and Determinative Value of a New Reaction of Pregnancy, Ostet. e ginec. **12:** 413, 1934.

The histidine test for pregnancy of Kapeller and Adler is positive in 98 per cent of pregnant women, beginning about the second month and becoming negative in the first week of the puerperium. The reaction is positive also in extrauterine pregnancy. The test becomes negative with the death of the fetus. The distinct advantage of this test is that it is simple and can be done in thirty minutes.

AUGUST F. DARO.

Rayner, E. B.: Heartburn in Pregnancy, Brit. M. J. **2:** 970, 1933.

The author ascribes heartburn to hypoacidity and believes that it is not always a symptom of hyperacidity. In a series of 45 cases at the Royal Simpson Maternity Hospital, the patients were divided into 3 groups. (I) Those not relieved by alkalies but by acid, 34 cases. (II) Those that were relieved by alkalis in relatively small quantities, 5 cases. (III) Those whose condition was aggravated by acid and not relieved by alkalies, 6 cases. A possible explanation for heartburn is that the stomach has a large margin of safety during digestion and reacts only when that margin is overstepped, as in hyperacidity. Conversely there is a relatively small margin for substances not present during digestion, as mucus, fatty acids, etc. In many hyperacidic and some hypoacidic stomachs the earliest reaction in each is heartburn. There is a fear or anxiety of heartburn; and anxiety lessens secretion and aggravates the hyposecretion, thus making a vicious circle. Dilute hydrochloric acid breaks up this circle. Heartburn is more frequent than the major toxemias of pregnancy and is very important from the patient's standpoint, even though it does not endanger her life. Hydrochloric acid should always be given a trial.

F. L. ADAIR AND I. BROWN.

Abramson, Roberts, and Wilson: Relaxation of the Pelvic Joints in Pregnancy, Surg. Gynec. Obst. **58:** 595, 1934.

Relaxation of the pelvic joints and particularly of the symphysis pubis is a normal accompaniment of pregnancy. Relaxation of the symphysis begins in the first half of pregnancy, progresses but slightly in the last three months, and is little affected by parturition. Retrogression begins immediately following delivery, and is usually complete by the end of three to five months.

The process of relaxation is physiologic and is probably the result of a hormonal activity.

Abnormal separation of the symphysis pubis occurs in about 25 per cent of the cases and probably results simply from an exaggeration of the normal physiologic process. Only exceptionally does trauma play any part.

Symphyseal relaxation is accompanied by an increase of pubic mobility and is frequently associated with characteristic symptoms resulting from instability of the pelvic joints.

Treatment is indicated to relieve symptoms and to prevent the development of a condition of chronic relaxation of the pelvic joints which is frequently responsible for a great deal of later discomfort among women who have borne children.

The key to the situation lies in prompt recognition of abnormal separation of the symphysis when present, and in order to detect this the obstetrician should include the symphysis pubis in his regular routine of examination of the pregnant patient both antepartum and at the time of delivery.

WILLIAM C. HENSKE.

Buddee, F. W.: The Ante-Natal Use of Quinine, Brit. M. J. 1: 1159, 1934.

Quinine decreases the power and increases the frequency of uterine contractions and therefore does not hasten delivery. In large doses it is a protoplasmic poison. The idiosyncrasy to quinine of some patients is discussed. Quinine hydrochloride was given in 5 gr. tablets every night. Labor began at varying times, within three to fifty-four days. There was no relation between the number of doses and the duration of labor. Quinine acts as a stimulant and general tonic, in small doses; the patients feel well and are often improved. There were no cases of fetal intoxication. Incidence of infection is usually reduced because of the increased resistance. Idiosyncrasy against quinine often causes premature labor.

F. L. ADAIR AND I. BROWN.

Guidetti, Ettore: Maternal Diet and Fetal Reserve of Vitamine A, Ginecologia 5: 597, 1935.

The author determined by the Carr and Price reaction the amount of vitamin A in the neonatal liver of rabbits and guinea pigs, and found variable values, from seventeen to forty Moore units per gram. The fetal liver reserve is not influenced by a maternal diet rich in vitamine A and the reserve value, calculated in terms of units of Moore, is the same in fetuses born from animals on either normal diet or a hypervitamin diet.

AUGUST F. DARO.

Orru, M.: A Study of the Calcium-Potassium Constant of the Organs During Pregnancy, Folia gynaec.-demograph. 31: 403, 1934.

In experimental studies made on various organs during gestation, in comparison with normal controls, in regard to their calcium-potassium contents, the author demonstrates: (1) that during pregnancy there is a tendency in all the organs, and especially in muscle, toward a diminution in the concentration of the cations therein contained; and (2) that the diminution is not constant for all the elements considered; there is an alteration in the coefficient toward potassium in muscle, toward calciums in the liver. These variations may be due either to the needs of the fetus or to the labile character of electrolitics, which is generally found during pregnancy.

MARIO A. CASTALLO.

Guercio, F.: Magnesium in Normal and Pathological Pregnancy. Part I. Magnesiemia and Cationemia in Pregnancy, During Labor and the Puerperium, Folia gynaec.-demograph. **31:** 607, 1934.

Employing the method of Kalinikowa, the author has studied the magnesium content of blood serum of over 100 patients in all stages of pregnancy. He also studied calcium and potassium by the method of Kramer and Tysdall, sodium by the same method and the micromethod of Muller modified by Condorelli; the method of Bang modified by Cannavo was used for chlorides.

He found that magnesium during pregnancy is present within normal and physiologic limits.

The maximum is 3.61 mg. per cent and the minimum 2.31 mg. per cent.

The values diminish progressively approaching term and even more so during labor. It is not improbable that magnesium is utilized from the mineral reserves of the pregnant woman together with a progressive impairment of the organism of the patient; or the diminution in maternal magnesium may be due to fetal assimilation. Lorenzetti has found a progressive increase in fetal magnesium as pregnancy continues.

Also the cations sodium, potassium and calcium are not notably changed from the normal. There is a slight decrease in sodium as pregnancy goes on. Normal values of potassium are found with a slight increase toward the end of pregnancy, while calcium shows values always below the normal of 10.8 mg. per cent.

Magnesium values show no great increase in pathologic conditions of pregnancy except in cases of eclampsia, where the patients were gravely ill.

MARIO A. CASTALLO.

Guercio, F.: Phosphatemia in Normal and Pathological Pregnancy, in Labor and in the Puerperium, Folia gynaec.-demograph. **31:** 323, 1934.

The author has found that in the blood serum of normal pregnant women in various periods of gestation, in labor and in the puerperium, and in pathologic pregnancy (eclampsia, albuminuria, abortion, and pernicious vomiting), phosphorus values are within normal limits, even if somewhat elevated, with a slightly greater elevation during labor. During the puerperium the values return to normal. The author observed particular elevation only in two cases of eclampsia, gravely ill, due to the acidosis and the insufficient renal filter for phosphorus.

MARIO A. CASTALLO.

Róna, Andor: Decidual Reaction on the External Cervical Os, Zentralbl. f. Gynäk. **56:** 3108, 1932.

During the course of interruption of pregnancy in a thirty-six-year-old woman, a polypoid nodule the size of a lentil was noticed on the margin of the external cervical os. Histologically, this nodule proved to be typical decidual tissue. Decidual tissue has been found on the peritoneum, especially that of the intestines, on the ovary, in the fallopian tube, and on the cervical mucous membrane. Rarely, it is found in the vagina and in the lymph vessels of the pelvis. It is not uncommon to find decidual tissue in the upper third of the cervical canal, but very uncommon to find it on the external cervical os. There are many theories as to the etiology of the condition, chief among them being: developmental anomalies, influence of corpus luteum, and mechanical influences such as operative trauma and infectious processes. The clinical interest lies in the fact that decidual tissue on the cervix is one explanation of bleeding during pregnancy, especially the early part.

WILLIAM F. MENGERT.

Sjovall, A.: Decidual Reactions in the Tubal Mucosa in the Presence of Intrauterine Pregnancy, Acta obst. et gynec. Scandinav. **15:** 68, 1935.

The author examined the fallopian tubes of 84 women with an intrauterine pregnancy and found a decidual reaction in only 10 of them. Even in these cases the areas of decidual change were small and isolated. Hence, decidual reaction in the tube in the presence of intrauterine pregnancy is infrequent. The author believes that inflammatory reaction and toxic influences predispose to the formation of the decidua.

J. P. GREENHILL.

Petti, Andrea: Effect of Morphine and Paramorphine Upon the Gravid Uterus, Arch. di ostet. e ginec. **20:** 120, 1933.

Petti studied the action of morphine and paramorphine upon the gravid and nongravid uterus of the cat.

The action of morphine depends upon the dose given. Doses of 1/2500 or even 1/1000 gr. produced an increase in tone, and increase in the number of contractions, a diminution in amplitude and some irregularity, while doses of 1/100 gr. produced a complete loss of force without completely inhibiting the contractions.

Paramorphine in doses of 1/1000 gr. has a double action acting either like morphine or inhibiting the rhythmical contractions completely. The paramorphine always makes the contractions regular even when they were irregular before its administration.

JAMES M. PIERCE.

Sorrentino, Benjamino: Motor Dysfunctions of the Kidney Pelvis and Ureter During Pregnancy and the Puerperium, Clin. ostet. **37:** 321, 1935.

The author reviews the various theories of the etiology of urinary stasis during pregnancy and the puerperium. Hirsch, Weibel, Pestalozza, Zangemeister among others believe that urinary stasis and dilatation of ureter and renal pelvis were due to mechanical factors, whereas Kehrer in 1912 and Rumpel in 1921 proposed the dynamic theory as a causative factor.

In a preceding paper the author was able to show on 136 cases that the mechanical factors play little if any part in determining the motor function and the alteration of the kidney pelvis and ureter during pregnancy.

His present work was performed by injecting an indigo carmine preparation (Merck) intravenously and observing its escape from the ureteral opening by cystoscopy. This procedure he calls chromocystoscopy. In a kidney that functions normally the elimination of the color is initiated after three to five minutes, reaches a maximum color intensity after ten minutes, maintains such intensity from ten to fifteen minutes and then gradually decreases until the elimination ends after thirty minutes. During pregnancy and the puerperium he was able to show curves of elimination that greatly differed from the normal type. The initial appearance of the color may be retarded, the elimination terminating quickly, without reaching maximum of color intensity, which he calls "short elimination." The initial appearance may be retarded without reaching a maximum intensity of color, yet the ejaculations are always of the same intensity and quality of color—the latter form he calls "monotonous elimination." On the other hand, the initial appearance may be retarded, the maximum intensity of color never reached, but the elimination period may be longer than normal—this he calls "prolonged elimination." He describes the character of the ejaculation and its significance.

The author concludes by affirming the importance of chromocystoscopy in the study of pyelo-ureteral function during pregnancy and the puerperium. It can

reveal many motor disturbances when abnormal types of ejaculation and abnormal curves of elimination of color are present.

AUGUST F. DARO.

Kersley, G. D., and Mitchell, D. A.: A Note on the Anemias of Pregnancy, Brit. M. J. **2**: 720, 1934.

The authors stress the importance of recognizing the presence of anemia in pregnancy before it reaches a dangerous degree unnoticed because of its insidious onset and course. This is most likely to occur in the last trimester of gestation.

The anemias may be subdivided into five kinds: the common microcytic type, the more rare megalocytic or pernicious type, anemia due to hemorrhage, anemia due to hemolysis following sepsis, and last, the rare idiopathic hemolytic anemia of pregnancy.

The microcytic anemias, which arise from a break in the chain of red cell development or erythron at the level of the normoblast, are due to the lack of iron usually associated with deficient absorption due to hypochlorhydria. The treatment consists of administration of iron in large doses.

The megalocytic anemias, in which a break in the erythron occurs at the level of the megaloblast, need not be accompanied by an achlorhydria and are spontaneously relieved by parturition. Treatment in pregnancy consists of administrations of liver with or without iron.

In the other types of anemia, where little is known of the cause, treatment consists of blood transfusion and, if the patient's condition warrants it, immediate induction of labor or cesarean section.

F. L. ADAIR AND I. C. UDESKY.

Schultz, Willi: The Pseudo-Anemia of Pregnancy, Arch. f. Gynäk. **157**: 110, 1934.

Carefully carried out examinations of the blood of nonpregnant women show that the lower level of normal range is 70 per cent for hemoglobin and 3,500,000 red blood cells. In 30 to 40 per cent of healthy women, these values are decreased slightly. This is due to an increase in blood plasma. These decreases are harmless and without significance. The author divides all anemic pregnant women into three groups: First, the true pseudoanemias of pregnancy; 30 to 40 per cent of all healthy women are found in this group. The hemoglobin is between 60 and 69 per cent and the red blood cells between three and three and one-half million. The color index and blood picture are normal. This condition is harmless and requires no therapy or consideration. In the second group are the essential anemias of pregnancy. This condition is a true blood dyscrasia and is uncommon. The hemoglobin is under 60 per cent and the red blood cells under three million. This condition is easily controlled by iron therapy. The pernicious type of anemia of pregnancy, which is rare, constitutes the third group. The color index is always less than one. In all other respects this condition resembles true pernicious anemia and responds to liver therapy. In the most rare types of aplastic anemias, only blood transfusions offer relief. The author does not believe that patients pass from one group into the other.

RALPH A. REIS.

Siegel, M., and Singer, B.: Occurrence of Tubercle Bacilli in the Blood of the Umbilical Cord and in the Newborn Infants of Tuberculous Mothers, Am. J. Dis. Child. **50**: 636, 1935.

Cases of undoubted congenital tuberculosis in stillborn or newborn live babies have been reported in literature. There is evidence that the tubercle bacilli

might be transmitted by way of the umbilical vein more frequently than is suspected. Cases have been described in which bacilli were found in the fetus in the absence of visible lesions and the same holds true for the placenta. The writers in this study investigated the possibility of detecting tubercle bacilli in the cord blood. In 15 cases studied in this respect one positive culture was obtained. The placenta in this case had a necrotic tuberculous area showing caseous masses in the placental sinuses. The infant was born prematurely in the seventh month, weighing 1100 gr., dying three hours after birth. No evidence of tuberculosis could be discovered in any of the various fetal tissues examined microscopically.

HUGO EHRENFEST.

Mahon, R.: The Obstetrical Prognosis of Large Uterine Fibroids, Rev. franç. de gynéc. et d'obstét. **29:** 1041, 1934.

According to Mahon the prognosis of large uterine fibroids from the obstetric point of view is not unfavorable for the mother or the child. Hence there is no justification for prophylactic interference. The physician should not interfere but he should be prepared for action when this becomes necessary. There is no parallelism between the size of the fibroid and the complications which may arise during pregnancy or labor. A diagnosis of necrobiosis of a fibroid during pregnancy is not an indication for intervention. Many women who have necrobiosis of uterine fibroids during pregnancy go through their pregnancy and the puerperium without symptoms. Most symptoms which arise as the result of this complication yield readily to rest in bed and an icebag. However, when septic necrosis occurs, an immediate hysterectomy should be performed. When a fibroid is found blocking the exit of a fetus, nothing should be done until the end of pregnancy. The amount of dystocia of a fibroid should not be judged until the patient has had a test of labor. Exceptionally, surgical intervention in the form of a cesarean section may be necessary. This should usually be followed by a hysterectomy. Occasionally, however, one may perform a cervical cesarean section followed by a myomectomy. If symptoms of infection arise during the puerperium, it is best to perform a hysterectomy. In summary it may be said that a physician should conduct himself as an obstetrician during pregnancy and as a surgeon during labor and the puerperium.

J. P. GREENHILL.

Lantuejoul, P.: Nine Myomectomies During the Course of Pregnancy and the Puerperium, Bull Soc. d'obst. et de gynéc. de Paris **24:** 275, 1935.

During the last fifteen months, 12 women were operated upon for fibroids of the uterus during pregnancy and the puerperium in Brindeau's clinic. Three of these women had hysterectomies whereas the remaining 9 had only myomectomies. Four of the myomectomies were performed during labor after extraction of the child by cesarean section. Two myomectomies were performed after labor, one through the vagina and the other by the abdominal route. Three patients had myomectomies during pregnancy before term.

The author emphasizes that myomectomies in general are simple to perform and have a good prognosis. Of the 3 women operated upon during pregnancy, only one aborted. This operation was performed at the fifth month and the fibroid which was removed weighed 11 pounds. There was one case of embolism in this series, in a patient who not only had a large fibroid but also placenta previa and a serious hemorrhage.

J. P. GREENHILL.

Rhemann, F.: The Question of Myomectomy During Gestation, Monatschr. f. Geburtsh. u. Gynä. **99:** 298, 1935.

In the opinion of Rhemann conservatism is indicated when fibroids are found during pregnancy, especially when no disturbing symptoms are produced. However, when symptoms arise because of the presence of fibroids, the fibroids should be enucleated during pregnancy, especially in young women. This operation is indicated even should an abortion follow the operation, because the patient can again become pregnant. Fibroids which are cervical or subperitoneal should especially be removed, because these tumors endanger the pregnancy and frequently necessitate the subsequent removal of the uterus. If, during the puerperium, fibroids undergo necrosis and infection, an operation should be performed. Women who had myomectomies during pregnancy should be delivered in a hospital.

J. P. GREENHILL.

Fujita, Y.: Beriberi Complicating Pregnancy and Puerperium, Jap. J. Obst. & Gynec. **17:** 461, 1934.

Generally speaking, women rarely suffer from beriberi in comparison with men. Yet the occurrence of this disease during pregnancy and the puerperium is not uncommon. Fujita reports 39 cases of this disease, which is due to deficiency of vitamin B. The symptoms include disturbances in the circulatory system, derangements in the nervous system, edema, abnormalities in the gastrointestinal system, and disturbances in various reflexes of the body. In most of the author's cases the disease manifested itself during the summer and early autumn. In the majority of cases the patients were affected during the latter part of pregnancy or during the puerperium. Premature labor often sets in. The mortality is generally given as between 9 and 13 per cent. However, only one of the author's 37 cases who were treated, died. Among the 27 women who had the disease during pregnancy, 7 of the babies died.

The disease may be prevented by people who live on rice by hulling the rice to leave the embryo bud, or they may take an additional supply of vitamin B. In order to overcome the disagreeable symptoms of beriberi it is essential to administer large amounts of vitamin B.

J. P. GREENHILL.

Sze, T. S.: Pregnancy Polyneuritis, Chinese M. J. **48:** 651, 1934.

Pregnancy polyneuritis is probably a diet deficiency disorder and not a toxemic manifestation. Rational therapy should be directed to supplying the deficiency in the form of a vitamin-rich diet, especially in B content. Prophylaxis consists in supplying abundantly the vitamin, particularly the B complex, in the form of a high protein diet and in avoiding restraint of eating vegetables after puerperium as is common practice among Chinese patients.

C. O. MALAND.

Ueno, J.: Experimental Study of the Effects of Vitamine B on the Female Genital Organs, Jap. J. Obst. & Gynec. **17:** 388, 1934.

In animals in which a deficiency disease is produced by lack of vitamin B, procreative ability is decreased and some of the animals become sterile. If a pregnancy does occur, abnormalities frequently follow. These may be in the form of uterine hemorrhage during pregnancy, intrauterine absorption of the

fetuses, early interruption of pregnancy, uterine atony, disturbances in involution, etc. During the disease the fetuses are hampered in their development. Many fetuses are born dead and those that are born alive are small and weak.

J. P. GREENHILL.

Fraymann, S. A.: Myelitis Complicating Pregnancy and Labor, Monatschr. f. Geburtsh. u. Gynäk. **99:** 210, 1935.

Myelitis becomes a complication of pregnancy and labor not because it represents an infection but because it produces a toxemia and results in hemorrhage into the gray and white substance of the spinal cord. Likewise it results in degenerated changes which are the result of a toxemia. If myelitis occurs during the first half of pregnancy, the latter should be terminated. However, if it occurs in the second half of gestation the pregnancy may be permitted to continue to term. The treatment of myelitis during pregnancy is the same as it is for pregnancy toxemias, namely, abundant venesection, removal of cerebral spinal fluid, and hunger. The author suggests that a better term for myelitis is "Myelopathia gravidarum toxica haemorrhagica."

J. P. GREENHILL.

Kolbe, L., and Szekacs, A.: The Value of the Flocculation Reactions for the Demonstrations of Syphilis During Pregnancy, Arch. f. Gynäk. **157:** 214, 1934.

The authors believe, as a result of their studies, that the Kiss reaction as well as the Kahn test are well suited for the determination of the presence of syphilis in pregnant or puerperal women. Both tests will disclose latent syphilis more frequently than will the Wassermann reaction. This latter test, however, is more specific even though it is less sensitive. The technic of the Kiss test is as simple as that for the Kahn test and both tests can be completed in a short time. Both may serve as controls for the Wassermann test but may also be used alone, especially if a careful history is obtained, and if the patient is carefully observed for signs and symptoms. The authors feel that these tests should be repeated in the puerperium.

RALPH A. REIS.

Spiegler, R., and Hartung, W.: Gonorrhea and Pregnancy, Monatschr. f. Geburtsh. u. Gynäk. **99:** 41, 1935.

Among 17,578 labor cases in Seitz's clinic, Spiegler and Hartung found gonorrhea during labor in 260 women, an incidence of 1.48 per cent. In addition, 280 women or 1.59 per cent had previously had gonorrhea but had no signs of it during labor. More than two-thirds of these women were unmarried and were primiparas. The puerperium was completely normal in only 50.8 per cent of the positive cases and in only 57.9 per cent of the previously treated patients. However, only about half of the puerperal complications in these cases could be attributed to the presence of gonorrhea. Actual ascension of the gonorrheal infection occurred in 18.8 per cent of the positive cases and in 7.4 per cent of the previously treated patients. A gonorrheal conjunctivitis occurred in 3.8 per cent of the newborn and a nonspecific conjunctivitis was observed in 8.8 per cent. It was interesting to find that 9.8 per cent of the women who had active gonorrhea conceived again and gave birth to children. Among the treated patients, 56.8 per cent conceived for the first time after they acquired their gonorrheal infection. Of the total of 540 patients, 213 or 39.4 per cent became pregnant again after they were infected. Furthermore 17 of these women conceived after they had had definite inflammation of the tubes.

J. P. GREENHILL.

Books Received

ERKRANKUNGEN DER EIERSTOECKE UND NEBENEIERSTOECKE UND DIE GESCHWUELSTE DER EILEITER. Bearbeitet von F. Kermauner, Wien, und L. Nuernberger, Halle. Siebenter Band in Stoeckel's Handbuch der Gynaekologie. Mit 472 zum Teil farbigen Abbildungen im Text, 1014 Seiten. Verlag von J. F. Bergmann in Muenchen.

ANTENATAL AND POSTNATAL CARE. By Francis J. Browne, M.D., Professor of Obstetrics and Gynecology, University of London, etc. With 58 illustrations and 480 pages. J. & A. Churchill, Ltd., London, 1935.

JOHN WHITRIDGE WILLIAMS. By J. Morris Slemons. The Johns Hopkins Press, Baltimore, 1935.

GROWING SUPERIOR CHILDREN. By I. Newton Kugelmass, Attending Pediatrician of the Broad Street Hospital, New York, etc. Illustrated, 568 pages. D. Appleton-Century Co., New York, 1935.

REGIONAL ANATOMY, adapted to dissection. By J. C. Hayner, Associate Professor of Anatomy, Metropolitan Hospital, New York, etc. 687 pages. William Wood & Company, Baltimore, 1935.

DER GEBURTSTOD (Mutter und Kind). Von Dr. Sigismund Peller. Verlag von Franz Deuticke, Leipzig und Wien, 1936. 110 Seiten.

A B C OF THE ENDOCRINES. By Jennie Gregory, M.S. Foreword by Carl G. Hartman. Illustrated. With 126 pages. The Williams & Wilkins Company, Baltimore, 1935.

FASCIAE OF THE HUMAN BODY and their relations to the organs they envelop. By Edward Singer, M.D., Department of Anatomy, College of Physicians and Surgeons, Columbia University. With 24 original illustrations, and 105 pages. The Williams & Wilkins Company, Baltimore, 1935.

THE PATIENT AND THE WEATHER. By William F. Peterson, M.D. Vol. 1. Part 1. The Footprints of Asclepius. 127 pages. Edwards Brothers, Inc., Ann Arbor, Michigan, 1935.

LEHRBUCH DER GYNAEKOLOGIE. Von Professor Dr. W. Stoeckel, Universitaets-Frauenklinik zu Berlin. Fuenfte, neubearbeitete Auflage, mit 465 Abbildungen im Text und auf 66 farbigen Tafeln. 760 Seiten. Verlag von S. Hirzel in Leipzig, 1935.

PRACTICAL HANDBOOK OF MIDWIFERY AND GYNAECOLOGY. By W. F. T. Haultin, gynaecologist, Royal Infirmary, Edinburgh, etc., and Clifford Kennedy, assistant gynaecologist, Royal Infirmary, Edinburgh, etc. Second edition, with 356 pages. William Wood & Company, Baltimore, 1935.

FOR AND AGAINST DOCTORS. An Anthology, compiled by Robert Hutchison and G. M. Wauchope. 168 pages. William Wood & Company, Baltimore, 1935.

MOEURS ET PROSTITUTION. Par Marcel Rogeat. Les Grandes Enquêtes Sociales. Nouvelles Éditions Latines. 7 Rue Servandoni, Paris, 1935.

MALADIES DES FEMMES ENCEINTES. Par Henri Vignes. I. Affections du tube digestif, 318 pages avec 34 figures. II. Affections du foie, pancreas; maladies de la nutrition, parois abdominales, peritoine, 206 pages. Masson et Cie, editeurs, Paris, 1935.

THE CERVIX UTERI, with special reference to the development of cancer. By R. Francis Matters, Lecturer in Human Physiology and Pharmacology, University of Adelaide, etc. Illustrated, 197 pages. The Hassell Press, Adelaide, 1935.

Item

American Board of Obstetrics and Gynecology

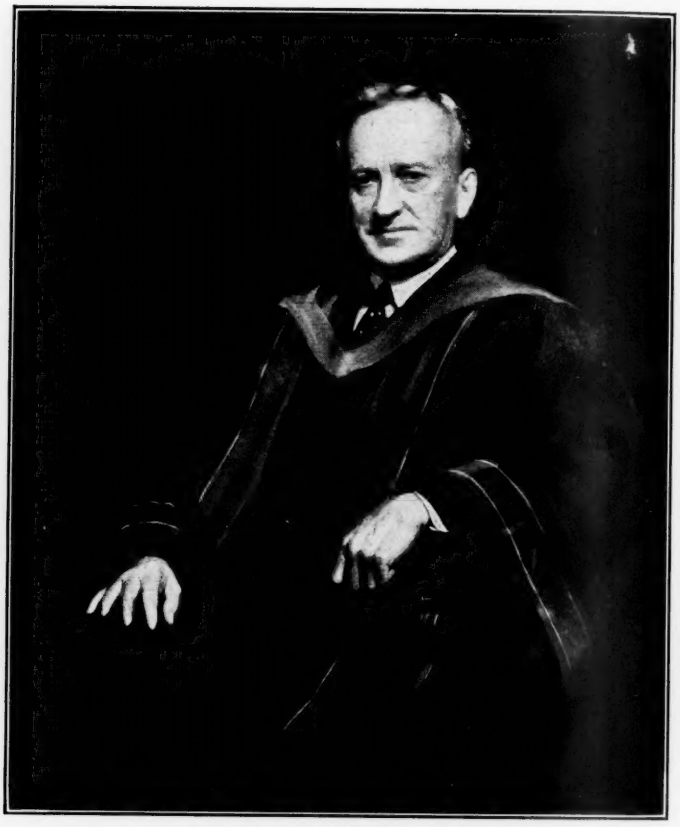
The oral, clinical and pathological examination of candidates for certification by this Board will be held in Kansas City, Missouri, on Monday, May 11, and Tuesday, May 12, 1936, immediately prior to the scientific session of the American Medical Association.

The annual informal dinner and general conference of Diplomates attending the American Medical Association convention will be held at the Hotel Kansas Citian, Kansas City, on Wednesday, May 13, at 7:00 P.M. At this dinner the successful candidates from the examinations of the two preceding days will be presented in person, and short addresses will be made by two members of the Board and two invited guests.

For further information, booklets, and application blanks, apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

C. Jeff Miller

We regret to announce the death on March 20 of Dr. C. Jeff Miller, of New Orleans, a member of the Advisory Editorial Board of the JOURNAL from the time of its founding and a valued contributor to its pages. A more extended memorial will appear in the May issue.



C. JEFF MILLER
1874-1936

American Journal of Obstetrics and Gynecology

VOL. 31 MAY, 1936 No. 5

IN MEMORIAM

CHARLES JEFFERSON MILLER
1874-1936

THIS distinguished surgeon died suddenly at his home in New Orleans on the morning of March 21. A coronary thrombosis suffered some two weeks before, was the cause of his premature death at the age of sixty-two.

The sad news came as a great shock to our medical world, for during the winter his customary activities had been maintained, and none could guess that his useful life was so near its close. A useful life indeed, one of great professional distinction, and of a wide and far-reaching beneficence!

Jeff Miller was a "Southern Gentleman" in the highest acceptation of that term; a fact ever modestly revealed in his carriage, his manners, and his speech. Courteous he was, downright and courageous.

He was born in the South, at Winchester, Tennessee. He was educated there and afterward at Terrill College, University of the South, at Sewanee; finally taking his degree in Medicine from the University of Tennessee. As he was then one of the youngest, he afterward became one of the most distinguished graduates of this school. It can truly be said of him that he was a brilliant student all his life—not only of medicine, but also of men and affairs.

Shortly after graduation, he settled in New Orleans, and it was in that city he spent the forty-two working years of his life.

From the beginning, Jeff Miller proved himself an admirable exponent of his profession, and notably in his chosen field of obstetrics and gynecology. Appointments of various kinds, both clinical and academic, followed in rapid succession, and he soon became known as a skilful and reliable surgeon, with a conspicuous *flair* for teaching and administration. And we may add that this rapid promotion was entirely self-earned, due solely to the qualities of the man himself.

In 1906 he was made President of the Orleans Parish Medical Society. His professional attainments were further recognized by the New Orleans Polyclinic and his appointment as Professor of Gynecology and Obstetrics in the Postgraduate Department of Tulane University. Early in his career he was associated with the old Presbyterian Hospital, since demolished, and later he became Chief of the Gynecological Service at Touro Infirmary, and head of an active service in Charity Hospital.

It was in these several institutions that he developed a careful, life-saving technique, and cultivated his natural teaching gift, which was eventually to find its full fruition when he was given the Professorship of Gynecology in Tulane Medical School. Already he had proved himself, both as a Surgeon and as a Teacher, the exceptional man, a prophet in his own country.

New Orleans, the city of his adoption, very early recognized in him not only the able physician, but also the qualities of a public-spirited, trustworthy citizen. He was made Chairman of the Annual Community Chest; the arrangement of no Carnival was complete without him; he was President of the Board of Trustees of the Howard Memorial Library, and for many years a Member of the Board of Control of the Leper Home of Louisiana. Recently he was the Campaign-Chairman for the erection of the Flint-Gooderich Hospital, in affiliation with Dillard University; a large scheme for the education and care of colored people.

These were but a few of his manifold activities, exercised as they were in the very midst of a strenuous professional life.

Is it any wonder that his city was proud of him?

Becoming eminent in this way at home, it was only natural that his influence should extend further afield, bearing the name and the fame of this Louisiana surgeon.

He was chosen as one of the founders of the American College of Surgeons, sat on its Board of Regents, and finally in 1930-31 became its President. In 1916 he was elected a Fellow of the American Gynecological Society, later served on its Council and was appointed its President in 1928-29; the following year he was President of the American Gynecological Club. Already he had acted as Chairman of the section of Obstetrics, Gynecology and Abdominal Surgery for the American Medical Association and also as President of the Southern Surgical Association. During the Great War he served as a Major in the U. S. Army Medical Corps. He became known in Europe as a Corresponding and Honorary Member of several of their specialist societies. At the time of his death he was President-elect of the South-Eastern Surgical Congress, meeting in his own city a few weeks ago.

It was indeed a full life, and full to the very end, for the above is but a mere sketch of his multiform activities, and gives no account whatever of the scrupulous attention to detail and the warmth of personal color with which he completed the picture.

Jeff Miller traveled widely, read extensively, and wrote much. It was in this way that his holiday was spent. Games of any sort, even the doctors' special recreations of golf and bridge, had small attraction for him.

Though he spoke of himself as a "stepchild of modern medicine, a mere clinician," his contributions to the science and practice of medicine were many and varied; and the communications themselves were all stamped by clarity, wisdom, and sound sense. Few men could so happily open or close a discussion.

The textbook *An Introduction to Gynecology,* published in 1931, is now in its second edition. Designed for the use of students, it is replete with sane advice, the result of accurate observation and of ripened experience.

His work was, of course, the large center of his life, nevertheless there was a wide circumference of interest in other things. There were the qualities of the artist in him; these specially manifest in his choice of reading, his love of music and beautiful things, and his literary gift. It is not too much to say that his "lay" addresses have been equalled by few in our profession. And last of all, the "High Gods" had endowed him with a great personal charm and a veritable genius for friendship.

C. Jeff Miller was a tower of strength to his profession; and in the wider world he will be long remembered as "a man ripened in wisdom walking as a physician."

Walter W. Chipman.

To this sincere tribute by a friend and colleague, the Editors desire to add and record their appreciation of Dr. Miller's constant interest and loyal support of the JOURNAL. He honored the Advisory Board as a member from its inception and was always ready and willing to give his advice and suggestion; he contributed many notable articles to the pages of the JOURNAL and stimulated the various members of his staff to do likewise. Dr. Miller's culture, his high literary ability, and his scientific attainments made his many and varied papers outstanding contributions to American medical literature. Dr. Miller was one of those rare characters whom it was a pleasure to have known and with whom it was an honor to have been associated.

George W. Kosmak.
Hugo Ehrenfest.

Original Communications

BLOOD CHEMISTRY AND RENAL FUNCTION IN ABRUPTIO PLACENTAE*

WILLIAM J. DIECKMANN, S.B., M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, the University of Chicago, and the Chicago Lying-In Hospital)

ALTHOUGH numerous obstetricians have reported the etiology, pathology, and treatment of abruptio placentae, no study of the blood chemistry and renal function has yet been published. The data which we have collected demonstrate the importance of vascular disease as the etiologic agent in many cases. They offer an explanation for some of the various phenomena, which will be described later, based on changes in the blood chemistry instead of a circulating "toxin."

The incidence of abruptio placentae varies from less than 0.5 per cent in some hospitals to 2.4 per cent in Edinburgh and 3.65 per cent in Manchester, England. There is a similar variation in the mortality rate which ranges from 3 per cent in most cities to 25 per cent in Shanghai, China.

A review of the literature, especially of the histories of patients who died, indicates that there was a tendency to bleed, and death was due to the persistent hemorrhage from the uterus.

DeLee, in 1901, made note of the hemophiliac-like nature of some of these cases and stated that the blood failed to clot in two cases. Williams reported one case with bleeding from the uterus for twelve hours after delivery and from the nature of the pathologic lesions believed it was due to a toxin similar to that found in the venom of the viperine snakes. Davis and McGee reported that in ten of the twelve fatalities in their series, death was due to continued bleeding from the uterus which could not be controlled by a pack or by clamping the uterine arteries in two cases.

Other authors have reported bleeding from abrasions of the vagina, from an abdominal incision, epistaxis, bleeding from the gums and subcutaneous ecchymosis, and have noted hemorrhages beneath the nails of the fingers and toes. I have seen two patients, in one of whom there was bleeding from the gums, the stomach, uterus, and into the subcutaneous tissues. In this patient blood failed to clot in the test tube. The other patient continued to bleed from the uterus, necessitating a hysterectomy. Both recovered.

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

This tendency to bleed cannot be the cause of the abruptio placentae, because we have observed four cases of pregnancy complicated by purpura hemorrhagica and there was no evidence at any time of a premature separation of the placenta.

A number of cases of anuria or oliguria associated with abruptio placentae also have been reported, and in many instances the suppression of urine caused the patient's death. The autopsy indicated that the anuria in a number of these patients was due to a cortical necrosis of the kidney. Ash contends that the cause of the cortical necrosis was an angioneurotic edema. Scriver and Oertel believe that the necrosis is the result of a terminal arterial segmentary collapse (vasoparalysis), with blood stasis and segmentary thrombosis.

In 1933, Ash collected 64 cases of cortical necrosis of the kidney. We have been able to add 14 more to date; several of these cases had been overlooked by Ash. Fifty-six of the 78, or 72 per cent, were associated with pregnancy. In 26 of the 56, or 46 per cent, the necrosis was associated with an abruptio placentae. Pregnancy was uneventful before the onset of the anuria in only 11 of the entire 56 cases. Authentic cases have also occurred in men. Sheehan reported several cases in men who worked in an ammunition factory.

Davis and McGee, as well as other authors, divided their cases into mild or partial (occurring usually near the end of labor), and grave or complete abruptio placentae (occurring most frequently before the onset of labor and associated in many cases with the Couvelaire type of uterus). In their series, 57 per cent of the patients had evidence of toxemia. Reports by other investigators state that from 24 to 100 per cent of the patients were toxemic.

The English obstetricians for many years have been classifying their cases into the toxic and nontoxic groups. The criteria for the former group have been the occurrence of one or all of the following signs: Edema, albuminuria, or hypertension. Kellogg has pointed out the connection between the kidney and certain cases of abruptio placentae. He was able to select a number of cases from a group of patients with separated placentas, which he called the "nephritic group." These patients, he stated, were generally characterized by relatively moderate parity. The nonnephritic group were older women, stringy, worn, and multiparous. He thought that an endometritis might be the main etiologic factor. High white counts were noted in both groups. Some of these patients also showed an increased bleeding and coagulation time. He stated that anuria in cases of abruptio placentae is a complication to be feared, and reported in detail a case associated with hypertension, anuria, and blood nitrogen retention. The patient received 22,560 c.c. of fluid and excreted only 634 c.c. of urine in five days. The nonprotein nitrogen rose to 120 mg. per cent during this period, but fell rapidly as the volume of urine increased.

The diagnosis of chronic nephritis in the majority of the reports always has been based on the presence of albumin in the urine. This is not correct because its presence does not necessarily indicate that the patient has nephritis. Furthermore, Brown has demonstrated that shortly after the abruptio placentae has occurred, whether it is of the revealed or concealed type, albumin appears in the urine. Likewise, in comparing the few cases in which blood analyses were made and, more

particularly, the pathologic examination of the kidneys, these patients do not have an acute or chronic glomerulonephritis, but a primary or essential hypertension.

We have been collecting statistics from various parts of the world on the incidence and mortality of the toxemias of pregnancy and abruptio placentae. There is some parallelism between the occurrence of the two conditions.

It is obvious clinically that there are two very definite types of abruptio placentae. (1) The separation of a normally implanted placenta at or near the end of the second stage or a placenta which overlaps the lower uterine segment and separates as the latter is lengthened by labor. (2) A separation occurring before or very early in labor, associated with vascular disease. In both types the normal degenerative changes in the vessel walls of the uterus are important factors.

Evidence of toxemia constitutes a systolic blood pressure of 140 mm. Hg or more, occurring on two or more days before labor or within the first ten days after delivery. Many of the patients were first seen in shock, but hypertension usually developed during the puerperium. However, with this criterium, we have undoubtedly included several toxemic patients in the nontoxemic group.

We have been able to study 58 cases of abruptio placentae. Forty-five of these cases occurred in the last four and one-half years during the delivery of 11,922 patients, an incidence of 0.37 per cent. Forty, or 69 per cent, of the 58 cases were toxemic, according to our criteria. This group is designated as "A" and the nontoxemic group of 18 cases as "B."

We have usually associated a Couvelaire type of uterus with the toxemic type, but while 11 were found in this group five were also found in Group B. The onset of symptoms in both groups occurred before labor in two-thirds of the cases. In Group A, 18, or 45 per cent, occurred between twenty-six and thirty-three weeks of gestation, and in Group B, 4, or 22 per cent. There were 70 per cent of Group A and 55 per cent of Group B between twenty-six and thirty-seven weeks of gestation.

The number of stillbirths and neonatal deaths was 28, or 70 per cent, in Group A, and 8, or 44 per cent, in Group B.

Weights for the infants were available in 28 cases in Group A, and 12, or 43 per cent, weighed less than 2,000 gm. In 16 cases in Group B, 2, or 13 per cent, weighed less than 2,000 gm. The fetuses in the toxemic group are below the normal weight for the period of pregnancy probably because the normal degenerative processes, plus the vascular disease, decrease the caliber or even obliterate some of the uterine vessels, resulting in either event in a decreased blood flow through the placental sinuses. Even if the pregnancy in these patients with primary hypertension continues to term, the babies are usually small.

In the toxemic group, 20 per cent were over thirty-four, while in the nontoxemic group, 39 per cent were over thirty-four years of age.

In Group A, 14, or 35 per cent, were primiparas, as contrasted with the other group in which there was only one primipara.

Urinalyses were made for the presence of albumin in 28 cases in Group A, and three cases in Group B. It was found to be present in all of them. Similarly, edema, more marked than that for normal pregnancy, was noted in 18 of the toxemic, and in none of the nontoxemic group.

In Group A there was a previous history of a toxemia of pregnancy in nine cases; in Group B there was none.

A marked anuria or oliguria was noted in three patients, but the use of blood transfusion and parenteral fluids cured these findings and probably acted as a valuable prophylactic against the suppression of urine in the others.

To summarize, a division of cases on the basis of the height of the blood pressure reveals additional significant differences between widely separated conditions. A comparison may be made in the period of gestation, fetal mortality and weight, age of the patient, parity, albuminuria, edema, and previous history of toxemia. It is apparent that there are two types of abruptio placentae, a vascular, hypertensive or toxemic type and a nontoxemic type. In either group the separation of the placenta may be partial or complete, the hemorrhage internal, external or combined, and the symptoms and signs may be mild or severe.

There was no maternal mortality in these 58 patients. One private patient died of a rupture of the uterus and was not included because of a difference in opinion as to the diagnosis of abruptio placentae.

In Table I are listed the systolic and diastolic blood pressures of both groups for various periods before and after delivery. Many of the patients in Group A, in spite of the shock, had a definite hypertension. In a number of them, although the systolic blood pressure was above 100, there is a tremendous drop if the post-

TABLE I. BLOOD PRESSURE IN MILLIMETERS OF MERCURY

RANGE	TOXEMIC			NONTOXEMIC	
	ADMISSION	POSTPARTUM 10 DAYS	POSTPARTUM 3 MONTHS	ADMISSION	POSTPARTUM 10 DAYS
			Systolic		
70-99				4	2
100-139	12	10	17	13	8
140-149	7	4	1		1
150-169	8	10	1		
170-199	9	6	2		
200-229	4	2	1		
			Diastolic		
20-59		1		3	1
60-79	5	4	10	10	7
80-89	5	8	5	2	2
90-99	10	4	2	2	
100-129	17	14	4		
130-159	3	1	1		

partum blood pressures are taken as criteria for the patient's normal pressure. This may explain the shocklike state which many of these patients present, but with a systolic pressure of more than 100. It is obvious that a drop in pressure from 200 to 120 is just as serious to the patient, if not more so, as a drop in a normal individual from 120 to 60. In Group B a number of the blood pressures were definitely in the shock range. The figures for the diastolic pressures show these contrasts even better than those for the systolic. The large number of cases with a diastolic blood pressure over 100 is quite marked in Group A.

In Table II are listed the figures for hemoglobin. The determination on admission is not an exact index of the patient's hemoglobin because following hemorrhage there is first a blood concentration and later a dilution. The subnormal hemoglobin after delivery, despite massive transfusions, indicates better the marked anemia which must have been present. In those patients who were transfused, the average amount of blood per patient was 1,183 c.c. The patients in Group B on admission had a lower hemoglobin than those in Group A. This may be due to a fact which we have noted, that pregnant patients with vascular disease have a higher hemoglobin than that characteristic of normal pregnancy.

TABLE II. HEMOGLOBIN, GRAMS PER 100 C.C. OF BLOOD

RANGE	TOXEMIC			NONTOXEMIC	
	ADMISSION	POSTPARTUM 1-10 DAYS	POSTPARTUM 3 MONTHS	ADMISSION	POSTPARTUM 1-10 DAYS
5- 6.9				3	2
7- 8.9	2	8	1	3	5
9-10.9	5	7	1	1	3
11-12.9	3	11	3	1	5
13-14.9	1		10		2
Average	10.6	11.1	13.0	8.0	10.0

In Table III are listed the cell volume determinations. The findings are similar to those for the hemoglobin. We wish again to call attention to the determination of the cell volume because of its accuracy and ease of determination.

TABLE III. CELL VOLUME, PER CENT

RANGE	TOXEMIC			NONTOXEMIC	
	ADMISSION	POSTPARTUM 1-10 DAYS	POSTPARTUM 3 MONTHS	ADMISSION	POSTPARTUM 1-10 DAYS
20-24		1		4	3
25-29	3	9	1	1	6
30-34	3	5		1	3
35-39	3	6	4	2	6
40-44	2	3	5		2
45-49			7		
Average	33.8	32.2	42	27.6	31.5

In Table IV are listed the concentration of serum protein for both groups. The number of determinations for each group was small. They showed no significant

TABLE IV. SERUM PROTEIN, GRAMS PER CENT, BOTH GROUPS

RANGE %	ADMISSION	POSTPARTUM		
		1-2 DAYS	3-9 DAYS	3 MONTHS
4-4.9	1	1		
5-5.9	5	6	1	
6-6.9	6	3	6	5
7-7.9	3		6	11
8-8.9			3	1
Average	6.5	5.6	7.1	7.2

difference and were, therefore, grouped together. It is worth noting that a number of the determinations on admission were below 6 gm. per cent and even after delivery and blood transfusion a number were still low. A considerable amount of serum protein is lost with excessive hemorrhage, and although there is a reserve supply in the tissues, if the hemorrhage has been excessive or protracted, the concentration of serum protein may reach a level at which proper interchange of fluids in the tissues cannot occur. The result may be the formation of edema and oliguria, or if acute, shock and death.

In Table V are listed the concentrations of fibrin. Both groups are again placed in one table because there were no significant differences between them. The normal concentration of fibrin in pregnancy at twenty-six to thirty-six weeks ranges from 0.280 to 0.580 gm. per cent, with an average of 0.430 gm. per cent. The number of patients with subnormal concentrations of fibrin is striking.

TABLE V. FIBRIN, GRAMS PER CENT, BOTH GROUPS

RANGE %	ADMISSION	POSTPARTUM 1-2 DAYS
0.010-0.049	3	
0.050-0.099		
0.100-0.149	2	
0.150-0.199	2	
0.200-0.299	1	3
0.300-0.399	3	2
0.400-0.499		4
0.500-0.599		1

In Table VI are listed the blood nonprotein nitrogen for both groups. Although the series is small, the number of patients in both groups with a nonprotein nitrogen of more than 40 mg. per cent, is striking. The average for pregnancy is 25 mg. per cent.

TABLE VI. BLOOD NONPROTEIN NITROGEN, MILLIGRAMS PER CENT

RANGE	TOXEMIC			NONTOXEMIC	
	ADMISSION	POSTPARTUM		ADMISSION	POSTPARTUM
		1-10 DAYS	3 MONTHS		1-10 DAYS
15-19					1
20-29	2	6	12	3	3
30-39	1	6	8	1	4
40-49	2	1	1	3	1
50-54		1			1

In Table VII are listed the urea clearances in per cent of normal for both groups. The majority of the figures are more than 50 per cent, which we have taken as a lower limit of normal. The average for Group A is less than that for Group B.

TABLE VII. UREA CLEARANCE, PER CENT OF NORMAL TEN DAYS TO ONE YEAR AFTER DELIVERY

RANGE	TOXEMIC	NONTOXEMIC
30- 49	6	
50- 69	10	5
70- 89	7	1
90-109	4	2
110-139	3	2
Average	73	83

Plasma cholesterol determinations were made on a number of the cases, but there is no significant difference between the two groups and the normal.

If hemoglobin and hematocrit determinations are made on the patient's blood and on some of the bloody fluid obtained from the vagina, the figures for the latter are usually much less in cases of abruptio placentae, while in placenta previa the figures are almost identical. In cases of abruptio placentae, hemorrhage and coagulation occur in the uterus, with a squeezing out of serum from the clot. Thus the blood in the vagina is diluted with serum.

DISCUSSION

It appears probable that the majority of the cases of abruptio placentae are associated with a vascular disease which is only rarely due to a chronic glomerulonephritis. This hypertension may be caused or intensified by the pregnancy. In some cases the pregnancy apparently stimulates a latent hypertension to become active. The hemorrhage may be internal or concealed, external or revealed, or combined. The first is usually the more serious because the failure of the blood to escape from the uterus is due to the laxity of the uterine wall. This lack of tone of the uterus predisposes to further hemorrhage. Other minor factors are the placental site and the patency of the cervix. Thus blood is more likely to escape if the placenta lies low and the cervix is dilated.

Goodall described the changes in the uterine wall after delivery and stated that the vessels were obliterated by a degenerative process. Schwarz and McNalley confirmed this work and noted further that changes in the intima occurred in pregnancies between twenty-four and thirty-six weeks' duration. They felt that these vessel changes were of importance because in those cases which showed the most marked vessel change there was extensive infarct formation in the placenta. They also suggested that abruptio placentae could very easily occur in patients with hypertension because the degenerative changes, with consequent weakening of the vessel walls, would favor rupture and hemorrhage.

The amount of hemorrhage and the resultant pathology would depend on the size of the ruptured vessel, the site of the rupture, that is, whether it was in the decidua basalis or the uterine wall, and the blood clotting properties of the individual case. While we have no direct evidence, yet reports of cases of suppression of the urine subsequent to marked infarction of the placenta or abruptio placentae would seem to indicate that in some instances these conditions are identical, differing only in degree. For example, if a maternal vessel supplying a portion of the placenta is slowly obliterated, infarction will occur. On the other hand, if the obliteration is marked or if the vein is obliterated before the artery, it is possible for hemorrhage (abruptio placentae) to occur.

Williams, Willson and others believe this condition is due to a toxin originating either in the placenta or the fetus, which injures the vessel wall, resulting in hemorrhage and preventing clotting of the blood. This theoretical toxin, according to them, has properties similar to those found in the venom of some of the vipers. A more reasonable explanation is that if a normal process of degeneration of the vessel walls and endarteritis is occurring in the uterine wall, plus vascular disease, rupture and/or thrombosis of a vessel producing hemorrhage or infarction are quite likely to occur.

The prolonged bleeding time seen in some cases is probably due to the marked decrease of the blood fibrinogen. There are several possible explanations for this decrease. The blood fibrin can be reduced markedly by blood loss. Whipple and coworkers, and McMaster and Drury have demonstrated that plasmapheresis will cause a marked decrease in fibrin which, if it is continued long enough, renders the blood incoagulable. However, within a period of hours or a day at the most the blood fibrin returns to normal. The second possibility is that with the hemorrhage, fibrinogen may be mobilized at the site of the bleeding, and if the latter continues for any length of time, it may be possible for the blood fibrin to become abnormally diminished. Thus an example of mobilization is the low fibrin concentrations reported in cases of pneumonia with exudate. Here the fibrin is mobilized in the pleural effusion. A third possibility is that the low fibrin may be the result of liver damage. Whipple and coworkers have shown that the liver is the primary site of fibrin formation and that after prolonged chloroform anesthesia or other toxic agents which cause liver necrosis the fibrin decreases, and in some cases the blood actually becomes free of it. Likewise, after removal of the liver there is a fall in blood fibrinogen and, within twelve to twenty hours, from 20 to 50 per cent have disappeared from the blood. In all of these cases of abnormally low fibrin, hemorrhage from the mucous surfaces and incisions occurs. The low concentration of fibrin found in some cases of abruptio placentae is probably caused by an actual loss due to the hemorrhage and a mobilization of fibrin at the area of the placental separation.

The hemorrhage causes a loss of hemoglobin, serum protein and fibrin from the body. The immediate effect of hemorrhage has been discussed by Dieckmann and Daily, but the salient points which should be emphasized are that it requires day or weeks for the regeneration of hemoglobin and serum protein. With abnormally low hemoglobin and serum protein concentrations the tissues suffer from anoxemia and the proper interchange of water and salts cannot take place. In a few cases the serum protein concentration had been decreased to such a degree that the life of the patient was endangered.

We believe the anuria is due to a spasm of the renal vessels and also to a lack of available water for renal excretion caused by the hemor-

rhage. A vascular spasm due only to hemorrhage will probably not result in thrombosis and necrosis of the kidney tissue, but if the patient has a vascular disease in addition, damage to the kidneys may occur. The fact that in many clinics adequate amounts and proper administration of blood, hypertonic glucose and Ringer's solution have prevented the occurrence of cortical necrosis, and the rarity of anuria now, in contrast to the period previous to the use of hypertonic glucose, warrants this belief.

Since the renal function in the majority of our cases after delivery is more than 50 per cent of the normal, and there is no persistent nitrogen retention and the urinary sediment after delivery is essentially negative, we believe that these patients, even though the hypertension persists, do not have a chronic nephritis but an essential or primary hypertension.

Pregnancy in patients with a primary hypertension or secondary to a chronic glomerulonephritis rarely goes to full term. The placenta, usually early in the last trimester, becomes markedly infarcted with resultant fetal death, or an abruptio placentae occurs, which also usually results in fetal death. A history of abruptio placentae, repeated abor-

TABLE VIII. ABRUPTIO PLACENTAE

Sept. 3, 1933
3:00 A.M. Sudden pain in abdomen. Vaginal hemorrhage of 200 c.c.
5:45 A.M. Pulse 120. Temperature 36.4. B.P. 100/?. Patient is exsanguinated. Uterus is large, tender, and does not relax. No F.H.T.

		20% GLUCOSE—C.C. INTRAVENOUS	BLOOD TRANSFUSION C.C.	RINGER'S SOLUTION—C.C. HYPODERMOCLYSIS
6:40 A.M.	*Cesarean section.* B.P. 108/?. 700 c.c. blood clot which is equivalent to 2,000 c.c. blood	800	800	2,000
7:30 A.M.	Air hunger—shock			
11:00 A.M.	Pulse 86. B.P. 130/85.	500	600	1,000
1:20 P.M.	*Subtotal hysterectomy* because of persistent hemorrhage from the uterus	200	900	1,000
6:30 P.M.	Pulse 84. B.P. 145/85. Temperature 37. 12-hour total—urine 30 c.c.	1,500	2,300	4,000

Sept. 4, 1933
6:00 A.M. Temperature 38.2. Pulse 96. Respiration 28. Twenty-four-hour total—Urine 1,250 c.c. Intake 9,350 c.c.

		HEMOGLOBIN GM. %	HEMATOCRIT %	SERUM PROTEIN GM. %	FIBRIN GM. %
Admission	9/ 3/33	6.8	23	--	0.161
	9/ 4/33	7.7	23	5.0	0.440
	10/ 2/33	10.6	36	8.7	
	11/ 9/33	13.0	43		

tions during the third trimester, or premature labor should always suggest vascular-renal disease, providing the Wassermann reaction is negative.

The data presented in Table VIII illustrate some of the changes in the chemistry and also the management of a case of abruptio placentae. In spite of the large amount of blood and parenteral fluids which were administered, an anuria almost occurred, and there was no increase in the hemoglobin concentration, and the serum protein content was subnormal.

The renal function after delivery in a number of cases was markedly impaired, but in a period of months it returned to normal. Thus if the figure for the clearance obtained at ten days and three months or more are compared, it will be noted that a clearance of 38 per cent was increased to 72 per cent; of 15 per cent to 99 per cent, and of 51 per cent to 125 per cent. However, the reverse also occurred. Thus the clearance in one case decreased from 89 to 45 per cent, in another from 78 to 50 per cent, and in still another from 75 to 52 per cent.

The patients in the toxemic group almost always had evidence of toxemia in subsequent pregnancies; the premature separation or placental infarction was likely to recur or abortion or premature labor occurred. Our data are inconclusive, but we have a definite impression that abruptio placentae predisposes to lowered fertility.

SUMMARY

1. Patients with abruptio placentae may be divided into a toxemic, hypertensive, or vascular disease group and a nontoxemic group. In the former the majority of the cases are associated with a persistent hypertension, which may have been initiated or intensified by the pregnancy rather than with a true preeclampsia and eclampsia. The nontoxemic group is associated with local conditions in the uterus. These may be subinvolution due to multiparity or infection, abnormal implantation, faulty contractions of the uterus, etc.

2. The hemoglobin, hematocrit and serum protein concentrations are lowered proportionately to the hemorrhage. If the loss of these substances is great enough, death may occur as a result of tissue anoxemia and improper interchange of water and electrolysis.

3. The determination of the hemoglobin and serum protein concentration on admission does not, as a rule, give a true index of the volume of the hemorrhage or of the patient's condition.

4. The systolic blood pressure on admission may be 100 mm. or more, and yet the patient may be in shock.

5. The blood fibrin may also be reduced to a concentration which predisposes to bleeding from mucous surfaces, incisions, and the uterus.

6. The renal function is impaired in many cases but returns to normal after an interval of several months. These tests demonstrate that a chronic nephritis is not present.

7. The prevention or cure of the associated phenomena is the prompt, adequate, and continued administration of blood and parenteral fluids.

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DISCUSSION

DR. L. S. McGOOGAN, Omaha, Nebraska.—Dr. Dieckmann has presented a classification of abruptio placentae which is new at least to me. In the nontoxic group local conditions such as the site of implantation, the character of the endometrial bed, etc., in addition to the local vascular changes which occur normally at the placental site, are the etiologic factors. In the toxic group there are present the above-mentioned vascular changes, but in addition there is generalized vascular change which would tend to the production of infarction or hemorrhage.

As to the etiology of this generalized vascular disease, Dr. Dieckmann has mentioned that previous toxemia of pregnancy is important. He does not mention, however, other conditions in which vascular disease might be present, i.e., syphilis and diabetes. I have personally observed cases of abruptio placentae in both conditions and believe they must have played a most important rôle.

According to Dr. Dieckmann's blood chemistry studies, the vascular disease is not due to a chronic nephritis. I cannot believe that the majority of these cases are due to a primary hypertension. The cause of the pure toxemias, at present unknown, may in these cases be playing an important part, with its greatest expression occurring in vascular phenomena, and clinically expressed as a toxemia.

I am glad that Dr. Dieckmann has emphasized certain clinical findings; first, the presence of shock with the systolic blood pressure reading still above 100 mm. of mercury; and second, the tendency of the patient to bleed from surfaces of the body other than that of the uterus. He has stressed that this purpuric condition is secondary and not primary. In April, 1935, I reported two cases in the American Journal of Obstetrics and Gynecology under the title of "Secondary Purpura Hemorrhagica Complicating Pregnancy." The title really should be changed to "Abruptio Placentae With Purpuric Phenomena."

DR. RUDOLPH W. HOLMES, Chicago, Ill.—There are three periods in the history of premature detachment of the placenta when nomenclature led to misinterpretation of the condition. Rigby, about 1770, differentiated the two important antepartum hemorrhages. Placenta previa was designated by him as "unavoidable." "Accidental hemorrhage" connated the premature detachment of the placenta as we know it today. Following his description clinicians commonly regarded some ac-

cident as the cause. Braxton Hicks, about 1865-70, stressed the fact that the hemorrhage of premature detachment was "concealed." Goodell, in 1880, by the caption of his thesis accentuated the fact of concealment. As a result, in the years thereafter, if the bleeding was entirely concealed it was a case of detachment of the normally situated placenta; if external bleeding occurred the case was probably a high lateral placenta previa. The third error arose when the term "abruptio placentae" was coined, for nowadays clinicians are looking for a violent, sudden onset. In 1899, after debating the matter with professors of Greek and Latin in the University of Chicago, it was agreed that *ablatio placentae*, or *placenta ablata* expressed graphically the clinic entity.

I am still convinced that etiologically there are three types of ablatio: first, one due to an injury; second, one due to pathologic alterations of the uteroplacental union; and third, one due to some toxemia. My conviction is that the poisonous element is not closely allied to the eclamptic poison, each of these poisons having a peculiarly selective power. My inclination is to hold that the third cause, probably, is the most frequent etiology.

DR. DIECKMANN (closing).—Dr. McGoogan very kindly emphasized some points which I neglected to state. In regard to the type of vascular disease, it must be a different type from what we see in eclampsia. Whether you want to call it a chronic nephritis, vascular disease, or hypertension does not make a bit of difference except we should agree on what we mean by these different things. In the last few years I have accepted the internist's point of view that chronic nephritis does not mean chronic glomerulonephritis.

In regard to purpura, I have seen four cases in pregnancy, none of the patients having abruptio or bleeding.

I like the term *ablatio placentae* better than *abruptio*, but I like *premature detachment* better than either of the two.

With regard to the control of hemorrhage, I may say that the patient whose chart I showed had 1,400 c.c. of citrated blood and continued to bleed. I operated upon her myself and she had a Couvelaire type of uterus. We usually remove the uterus in women who have had several children. I had to remove the uterus by supravaginal hysterectomy about five hours after the cesarean.

Jones, Rathmell, and Wagner: The Transmission of Syphilis by Blood Transfusion, Am. J. Syph. & Neurol. **19**: 30, 1935.

The procedure of blood transfusion should be carried out by competent and well-trained men. Institutional work should be guided by a physician who is qualified and who should insist upon a minute examination of blood donors at frequent intervals for the presence of a syphilitic infection. There should be available at all times the facilities of a laboratory wherein the common serologic examinations of donor's and recipient's blood for the presence of a syphilitic infection are conducted. This examination should be made on the day of transfusion. Laboratory reports should be written, not telephoned, given to residents verbally, or relayed to nurses. Such reports should be made by a competent technician and should be attached to the patient's records at the time of transfusion. No physician should consider the transfusion of blood, except in the gravest emergency, unless the donor gives a history, physical examination and laboratory tests which are all negative for syphilis.

The authors do not agree with the statements of observers who feel that inactive syphilis may not be transmitted. All syphilitics are potential transmitters.

C. O. MALAND.

LATE RESULTS IN THE TREATMENT OF LEUCOPLAKIC VULVITIS AND CANCER OF THE VULVA*

FRED J. TAUSSIG, M.D., ST. LOUIS, MO.

THERE has been ample discussion in the past concerning the classification, pathology, and treatment of leucoplakic vulvitis and carcinoma of the vulva. Recently we have had interesting contributions by Adair and Falls upon this subject. Concerning the ultimate outcome of treatment, however, we have as yet but little information. German literature contains a few analyses of operative results but in this country the subject has scarcely been touched upon.

The present study of the final results in the treatment of these two conditions is based upon the outcome of 74 cases of leucoplakic vulvitis and 112 cases of carcinoma of the vulva seen during the last thirty years. Previous to 1915 only a few cases came to our notice and all of these were given only palliative treatment. During the last twenty years, however, a method of operative treatment has gradually developed that has given not only temporary relief but in a surprisingly large percentage of patients has led to permanent cures. Unfortunately a large number of the women with leucoplakic vulvitis refused any operative measures. In carcinoma of the vulva the number who refused treatment was smaller but approximately 25 per cent were in such bad physical condition or had such extensive involvement that nothing more than a simple vulvectomy could be done. If at present a radical operation can be done in 75 per cent of vulval cancers in spite of the fact that the disease was present for longer than a year and that many had palliative treatment elsewhere, it certainly speaks well for the possibilities of accomplishment by this method.

Between 1915 and 1930, I observed 45 cases of leucoplakic vulvitis. Eighteen of these refused operation. Practically all of these patients also refused any follow-up of their condition so that I am unable to state what percentage, if any, later developed carcinoma. One patient upon whom I could make examination after an interval of five years showed no appreciable change in the appearance of the leucoplakic vulvitis although the pruritus had become somewhat less. There remained then 27 patients upon whom I had done a vulvectomy in the fifteen years preceding 1930. In ten of these the lesions were limited to a small area and only a partial vulvectomy was performed. In the remaining 17 patients a complete vulvectomy was done including two patients in whom retroanal skin was removed by the double anal bridge method of operation (Fig. 1).

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

An analysis of the five-year results in these 27 cases showed that five could not be traced; two died before the five-year period had elapsed, one from postoperative embolism, and one from tabes. Seventeen of these patients had practically complete relief of their symptoms; and in three others there was only a small recurrent area that required merely local cauterization to bring about a cessation of symptoms.

In the ten-year follow-up of these cases we find 17 that come in this group, but during these additional years many were lost track of so that further data were available concerning only six patients. This made the record as follows: died 2; not traced in first five years, 4;

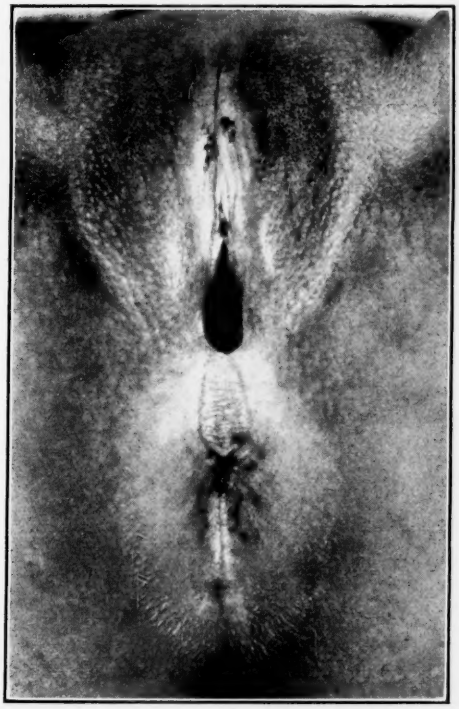

Fig. 1.—Leucoplakic vulvitis with kraurosis and involvement of a large area of perianal skin. This patient was operated by complete vulvectomy and removal of perianal skin leaving a bridge of tissue to either side laterally.

not traced between five and twelve years afterward, 5; cured for ten to fifteen years, 6. No failures were reported.

In the past five years I have had four patients upon whom it was necessary to do secondary surgical excisions for a recurrence. In two of these the recurrent lesions were in the vulvogluteal folds, and in the remaining two the perianal skin had developed a leucoplakic change.

In weighing in the balance the final results of vulvectomy in the treatment of leucoplakic vulvitis, we cannot deny that some of these patients complain of a disagreeable feeling of tightness about the vulval skin and

occasionally also of some irritation about the urethra from the scratching of the hairy skin to which it is approximated. Dyspareunia and pain on defecation due to vaginal and rectal postoperative stricture, formerly one of the chief drawbacks to these operative procedures, are no longer to be dreaded since I have been doing the posterior vaginal flap and double anal bridge operation. All in all, the operative results both immediate and late must be termed highly satisfactory. Since I have had but one operative death in 52 vulvectomies for leucoplakic vulvitis and that in a patient seventy years of age from embolism on the fourteenth day after operation, there can certainly not be said to be any special danger from this surgical procedure. I question whether any of the operations now being done to resect the local nerves or sympathetic plexuses can surpass these results either in the way of primary mortality or ultimate permanent relief. It is the generalized symmetrical type of leucoplakic vulvitis that gives us the most trouble, and here we must assume endocrine and neurogenic factors as the most likely cause. Resection of the tributary nerve supply should give temporary relief in such cases, but it remains to be seen how long the beneficial results of this nerve resection will last. It seems logical to suppose that as soon as the sensory nerves regenerate, the atrophic friable vulval skin will again be subjected to traumatism with a return of the old trouble. For this reason it is particularly important to study the late results of any method of treatment.

Coming now to carcinoma of the vulva, we are faced in our follow-up of cases with the fact that this is a disease not merely of old age, but of extreme old age. Approximately 60 per cent of the women were over sixty years and 30 per cent over seventy years of age. Naturally the normal life expectancy of such women cannot average more than about five years. It is therefore not fair to consider every death that occurs in the five- or ten-year period following operation as a failure to effect a permanent cure. Such a rule, justly applicable to cancer of the cervix with its average age of forty-five, cannot be extended to cancer of the vulva with an average of sixty years.

Out of 112 cases of vulval cancer under consideration in this review, 76 were seen before 1929. During this period a variety of procedures were employed: radiation, simple vulvectomy, vulvectomy with removal of superficial glands, and vulvectomy with double-sided Basset operation. A comparison of five-year results reported in 1929 and borne out by subsequent reports showed definitely the great superiority of the radical gland removal over any other measures. In this first series it showed 81 per cent five-year cures with the Basset operation compared to 30 per cent where only the superficial glands were removed, and no cures with radiation or simple vulvectomy.

Simple vulvectomy according to Kehrer in Germany will yield from 3 to 6 per cent five-year cures, and irradiation treatment according to Stoeckel's summary of 126 cases with 15 cures will give us, even with present improved methods of treatment, only 12 per cent of five-year cures. In my opinion it is no longer a matter of debate what is the best method of treating carcinoma of the vulva. If in operable breast cancer, radical surgery with gland removal is unquestionably accepted as the best method of treatment, then the same should also apply to cancer of the vulva. In the 36 patients observed since 1929, there were only nine in whom extreme old age, general physical condition, or advanced stage of the disease made it impossible to carry out a radical surgical excision. It was the general physical condition of the patient rather than the extent of the disease that served as an operative contraindication. The remaining 27 patients were subjected to a Basset operation.

This brings the total number of complete Basset operations done up to the present time to 43 cases. In four additional patients lymph glands were removed only on one side, or the Basset operation could not be completed because of invasion of the femoral vein by the cancer. Once the subsequent microscopic examination after a double-sided Basset failed to confirm the original diagnosis of a carcinoma. These five cases have been left out of consideration in the present study.

I have divided these 43 patients into three groups: (1) those operated upon ten or more years ago; (2) those operated upon five or more years ago; (3) those operated upon less than five years ago. The results are tabulated below:

TABLE I

YEARS OF OPERATION	TOTAL NO.	OPERATIVE DEATHS	DIED RECURRENT IN FIRST 5 YEARS	DIED RECURRENT BETWEEN 5 AND 10 YEARS	DIED OF OTHER DISEASES BETWEEN 5 AND 10 YEARS	DIED AFTER 10 YEARS	LIVING AND WELL	NOT TRACED
1915-1925 (Oct.)	12	0	3	1	3	3	2	0
1925 (Oct.)-1930 (Oct.)	11	1	3	1	0	–	6 (One recently recurrent)	0
1930 (Oct.)-1935	20	1	3	–	–	–	15	1
Total	43	2	9	2	3	3	23	1

In the immediate results of this method of treatment it will be noted that there were two primary deaths, one on the ninth day from sepsis and one on the twelfth day after operation from embolus. It is worthy of mention that in spite of long operations often lasting two to three hours, done upon old and often debilitated patients, there were no deaths

from shock or hemorrhage. The operative mortality was therefore 4.6 per cent, assuredly low enough not to deter any competent surgeon from undertaking this extensive procedure.

If we consider now the 23 patients operated five or more years ago, we find one operative death, six who died of recurrences, one living but recently recurrent, and 15 who lived five years free of recurrence, *a five-year curability of 65 per cent.*

Out of 12 patients operated upon ten years or more ago four died of recurrence during this period. Three patients died of other causes without local recurrences before the ten-year period had elapsed. Leaving these three patients out of the calculation, we have left nine patients, five of whom lived for ten or more years free of recurrence, *a ten-year curability of 55 per cent.* Of these five patients, one died after eleven years of local recurrence, one died of senility twelve years later not recurrent, and one died of cancer of the cervix fifteen years later without local recurrence, leaving two living and well today, one eleven years and the other twelve years since operation.

The necessity of removing the tributary lymph glands is evident from the high percentage of cancerous involvement. In 26 out of the 43 Basset operations one or both sides showed metastases, an average of 60 per cent. In some of the remaining cases a small cancer metastasis might readily have been overlooked.

The advantage of blocking off the spread of the cancer by a thorough removal of the tributary glands is best witnessed by studying the recurrences. Out of 12 deaths from recurrence, three patients died of local recurrence, three of recurrence in the inguinal glands, two of distant metastases (brain, lungs) and in four insufficient data were available. We also had five patients who had small new cancers that appeared upon unremoved portions of leucoplakic skin about the vulva or anus. In these patients a secondary surgical excision was done and has been amply justified by the results obtained: one is living and well ten years since the second operation; one died recurrent seven years later, one died recurrent one year afterward, and two are of too recent occurrence to be considered. In none of these five cases was there any further glandular involvement or metastases to distant organs, indicating that this portal had been definitely closed by the Basset operation.

In illustration the following record is given: Mrs. L. McC., sixty-six years old, entered Barnard Free Skin and Cancer Hospital, Oct. 7, 1929, with an extensive carcinoma of the right labia and prepuce on a basis of leucoplakic vulvitis (Fig. 2). Vulvectomy was done October 8 and a double-sided Basset operation Oct. 22, 1929. She was free of recurrence until Aug. 4, 1931, when a small area of cancer 3 x 1 cm. above the urethra required excision. For four years more there was no recurrence. Then in July, 1935, an area of ulceration to the right of the anus was noticed. Examination showed a new carcinoma developing from the perianal leucoplakic skin that had not been completely excised (Fig. 3). This carcinoma

was removed by cautery excision two weeks ago. The patient is now in good condition, seventy-two years of age, six years after her primary operation and has a good chance of spending her remaining years without further recurrence.

In connection with this tendency to the development of new cancers in remaining islands of leucoplakic skin that have not been fully excised, we should give weight to the strikingly large number of patients in this group of forty-three patients, who developed cancers in other organs, either previous to or after the development of the vulval cancer. There

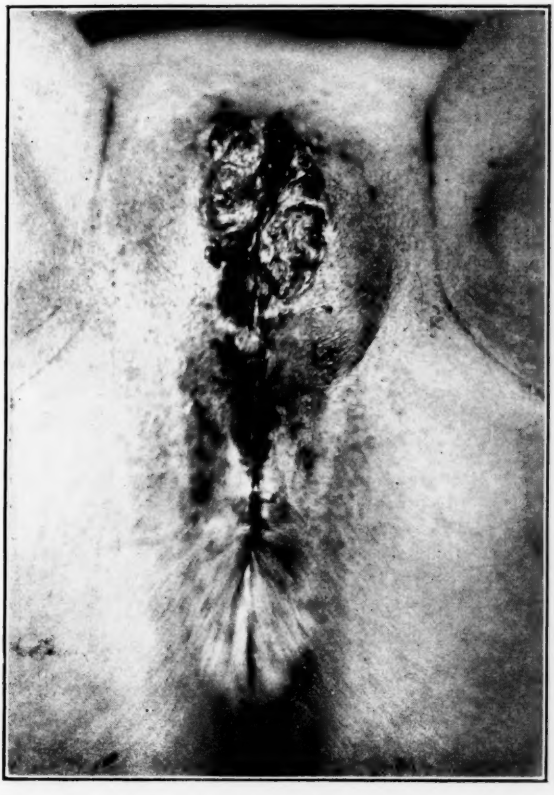

Fig. 2.—Carcinoma of the vulva developing on a basis of leucoplakic vulvitis with perianal involvement similar to Fig. 1. This carcinoma involved both labia minora and prepuce. This operation was done Oct. 7, 1929 followed by a double-sided Basset. A small local recurrence was excised in 1931 near the urethra. Patient remained well until 1935 (see Fig. 3).

were four such cases, two patients who had cancer of the cervix and two who had cancer of the breast. Since this is considerably higher than the average incidence for such a combination of these two cancers, it makes us wonder whether we should not pay more attention to underlying somatic factors in cancer etiology.

It was certainly a striking fact in my series of cases that when a portion of leucoplakic skin was for some reason not completely removed in operations for simple leucoplakic vulvitis, cancer never developed in

such a leucoplakic area. On the other hand, when such a leucoplakic island was left after operations for cancer of the vulva arising on a leucoplakic basis, we found that in the course of two to six years a new cancer developed upon such a leucoplakia in five out of approximately forty such combined lesions. It would seem from this that underlying constitutional factors are perhaps the basic cause of the cancer and the irritated leucoplakic skin merely "the match that starts the fire to burn."

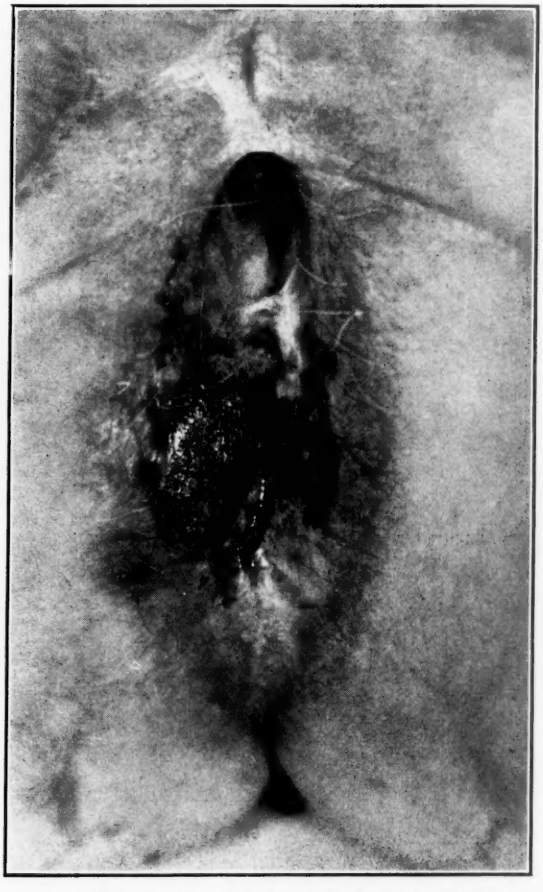

Fig. 3.—Same case as Fig. 2. No recurrence in former operative wound or groin. Development of a new carcinoma in July of 1935 from the unexcised portion of perianal leucoplakic skin. Local excision Sept. 23, 1935.

The essential points in this analysis of late results are:

1. Leucoplakic vulvitis is permanently cured by vulvectomy in all but a few cases; occasionally a secondary excision is required.

2. The age incidence of cancer of the vulva is so high that many patients die of other diseases before the ten-year period has elapsed.

3. The five-year curability of 23 Basset operations for cancer of the vulva was 65 per cent. The ten-year curability was 55 per cent.

4. With an operability ratio of 75 per cent and a primary mortality of only 4.6 per cent, the treatment of cancer of the vulva gives with the possible exception of cancer of the uterine body the most favorable prognosis of any form of malignancy in the genital tract.

5. The experience of the past six years has further buttressed the conclusions presented in my paper of 1929, that radiation, vulvectomy, and superficial gland operations with vulvectomy have no place in our treatment of vulval cancer except as palliative measures. Three out of four such cases can and should be subjected to the double-sided Basset gland excision with vulvectomy, and approximately two-thirds of these will remain well for longer than five years.

3720 WASHINGTON BOULEVARD.

DISCUSSION

DR. FRED H. FALLS, CHICAGO, ILL.—For the leucoplakic type of vulvitis we are all agreed that surgery should be done. On the other hand, there is no unanimity of opinion about the use of operative procedures in the carcinoma cases. Our experience however coincides exactly with that of Dr. Taussig. Women of from sixty to seventy-five years of age seem poor operative risks, but our experience has been that they stand operation very well. In patients who were not good operative risks we have done the two-stage operation.

We do not believe that radium should be used as a curative agent in these cases, but it is helpful to radiate with the radium plaque the skin of the inguinal canal before operation. Our plan is to use small doses of radium by the radium plaque method, moving the plaque along the inguinal canal, about 200 mg. hours to each side, about three weeks before we plan to do the Basset operation. We also follow up our operative procedures with x-ray therapy in all cases, paying particular attention to the radiation of the inguinal and iliac glands and the areas where metastases may occur.

We have had no serious discomfort from any of these vulvectomies, although sometimes the patients have complained of some tenseness. We have had one death in a case of carcinoma, but there have been no deaths in the primary operation for leucoplakia. There has been no recurrence in the cases we have been able to follow at the Research Hospital. It is very difficult to follow up cases that come into the Cook County Hospital, but none of the patients operated upon there have come back with recurrence.

DR. W. A. COVENTRY, DULUTH, MINN.—We have not done the radical operation but I intend to in the future. Removal of the inguinal glands only is a limited operation and the majority of the cases so treated will get metastases along the iliac vessels and die. Two of my patients died rather spectacularly. In one metastases developed along the iliac vessels and the patient died of hemorrhage, death occurring in a very few moments. In the other where we had dissected out Bartholin's gland and inserted radium into the cavity, the incision never healed and the patient eventually died of hemorrhage from the iliac vessels.

DR. TAUSSIG (closing).—These old women if possible should be given the benefit of a vulvectomy at least. Death from spreading cancer of the vulva is one of the most painful and terrible conditions that we have to face in cancer hospitals. Even where we do not dare to go after the glands in the inguinal region or where age or the condition of the patient makes it inadvisable, a vulvectomy should be done.

We used x-ray for a time as a preliminary to the operation and found no advantage to it. *A priori,* I hesitate very much to do anything to the inguinal skin that will further increase the tendency to necrosis. I do not know how to prevent some necrosis after these operations and we only rarely get primary union. I wish I knew some way in which we could hasten postoperative healing. Not that it leads to serious complications, but it means a long stay in the hospital, and sometimes requires skin grafting and plasties.

We have had six cases of Bartholin's gland carcinoma in our series. In five out of the six the inguinal glands showed cancer. I consider this location for carcinoma as distinctly less favorable than the type that develops from leucoplakic skin.

THE ETIOLOGY, DIAGNOSIS, AND TREATMENT OF EVISCERATION FOLLOWING LAPAROTOMY*

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THOUGH a properly performed laparotomy may be considered a comparatively safe procedure, there is hardly a surgeon of experience who has not occasionally encountered separation of an abdominal wound, with or without eventration of the omentum and bowels. This distressing and often fatal surgical accident occurs far more frequently than it may appear. There are, however, but few reports on this subject in the literature.

v. Gusnar found 11 cases among 2,310 laparotomies (0.5 per cent); Starr and Nason 15 among 2,455 (0.61 per cent). From the material of the Presbyterian Hospital and the Surgical Department of Columbia University in New York, Meleney and Howes collected 55 cases, an incidence of 1 per cent, but assume that the actual incidence may be twice as high. R. Colp has reported 26 cases among 2,750 laparotomies (0.94 per cent). During a period of three years 9 cases of wound separation were noted among 567 laparotomies (1.58 per cent) in the Department of Obstetrics and Gynecology of the State University of Iowa.

Thirty years ago Madelung reported 175 cases with the appalling mortality of 29 per cent. After enumerating all the possible causes, such as vomiting, coughing, sneezing, straining during bowel movement, restlessness, sudden movement of the patient, and occasional wound infection, he concludes that none of them satisfactorily explained this "accident," which could be neither foreseen nor prevented.

Ries states that the disruption is initiated by separation of the fascia because of the sutures breaking, the suture knots giving way, or the tissue being cut by the sutures, and that in most cases the separation of the deeper layers occurs soon after operation: "The deeper layer then granulates, but doesn't heal together because the abdominal contents push in between the granulating edges. The second steps take place days or weeks afterward when the skin also gives way."

Freeman also stresses separation of the peritoneum and fascia soon after operation and claims that it is the wedging of the omentum between the edges of the fascia which prevents the healing of the superficial layers and is responsible for the peritoneal symptoms, such as nausea, meteorism, and abdominal distress.

*Presented before the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, Omaha, Nebraska, October 10 to 12, 1935.

McCauliff is inclined to believe that the deeper layers give way during the first seventy-two hours because the peritoneum would otherwise heal, and remain closed to cover the bowels. The main cause for disruption, when the incision is made *through* the muscle, according to this observer, is the weakening of the muscle, whereas the higher frequency of disruptions following median incision* depends upon the fact that the fascial incision entirely lacks muscle protection.

The more recent studies of Halsted, Harvey, and Howes and collaborators, on the healing of wounds in relation to the use of catgut and silk, as well as experiments of Kraisel and Meleney to determine the time of catgut digestion, seem to support the observations of Ries. These investigators have encouraged the use of non-absorbable sutures for the fascia in order to minimize the danger of wound separation by shortening the critical "latent period," before the scar has become firm.

According to Sokolov, who, in 1931, reported 725 cases of wound separation, it seems that the use of catgut actually increases this danger. Among 50 cases of wound separation reported by Meleney, silk had been used for the closure of the fascia in only one case. The same situation holds true for the 25 cases reported by Eliason and McLaughlin. Many surgeons in Germany and Austria therefore adhere to the use of silk. I saw only three or four such accidents among several thousand laparotomies during twenty years as a staff member of the II. Frauenklinik in Vienna. Appalled by the incomparably higher frequency of this complication when catgut is employed, I have returned to the use of silk for the closure of the fascia.

Though suture material apparently has some bearing on the incidence of wound separation, it seems very doubtful whether one is justified in giving it too much consideration. Many thousands of laparotomies closed with catgut have healed properly, and, on the other hand, laparotomies closed with silk have given way. Even if we should agree with Ries that in these cases the silk sutures have cut through the tissue, and assume that when catgut was used the sutures had been digested before the incision in the fascia was firmly united, there is no adequate explanation for the fact that the separation did not remain limited to the fascia. The occasional development of large incisional hernias soon after operation shows that disruption does not necessarily follow the separation of the fascia, if in the interval the scars in the subcutaneous tissue and skin have become strong enough to withstand the intraabdominal pressure.

Although there is no doubt that the separation of peritoneum and fascia is the first step, avoidable in many instances by the use of a non-absorbable material with tensile strength unreduced over a period of many days, it seems obvious that the disruption of the subcutaneous tissue and skin is due to an impairment of proper healing. In fact, one is impressed by the conspicuous absence of any healing reaction, the subcutaneous tissue of the ruptured wound presenting the aspect of a fresh incision although the operation has been performed a week or ten days previously (Cases 1, 2, 3, 4, 7, 9).

*Among 181 cases of disruption, collected from the literature, in which the location of the incision was designated, 151, i.e., 80 per cent, occurred following median laparotomy between symphysis and umbilicus.

Poor nourishment, anemia, cachexia, advanced age, the presence of malignancy, syphilis, tuberculosis, jaundice, diabetes, and kidney lesions have been suggested as possible causative factors, depending upon which was present in the individual case. It has, however, never been proved that any one of these conditions, with the exception of diabetes, would seriously impair the process of healing.

Seven of our nine patients were otherwise healthy, not anemic, but noticeably obese women. Their ages ranged from thirty-two to sixty-four years. Sugar was found in the urine of one of the first five patients, but she was not considered diabetic. A sugar tolerance test taken seventeen months later revealed normal conditions. This does not, however, exclude the possibility that she may have had a hyperglycemia at the time of operation as it is known that injury may produce hyperglycemia in individuals with labile sugar metabolism.

Very much disturbed by the startling frequency of wound separations, five of which (one fatality) had happened within fifteen months, an attempt was made to ascertain, if possible, the reason for the discrepancy in the results at the clinics in Vienna and Iowa City. The following points seemed to be of importance:

	IOWA CITY	VIENNA
Suture material	Catgut	Silk
Food, as a whole	Rich	Moderate
Quality	Richer in carbohydrate	Poor in carbohydrate
Frequency of diabetes	Conspicuously above average	Average

From the foregoing it would seem imperative to give special attention to the sugar metabolism.

The findings in the following four cases of wound separation seemed to indicate that we had reached the correct conclusion. In Case 6, although the patient's urine was sugar-free on admission, the tolerance test on the twenty-second day following eventration revealed a mild diabetes with a high renal threshold. The length of time which had elapsed between the eventration and the test eliminated the possibility that the disturbance in the sugar metabolism might have been a temporary condition caused by the glucose administered postoperatively. In addition, healing of the secondarily infected laparotomy wound and of a burn on one leg was slow until the patient had been placed under diabetic management. Patient 7 was suffering from a severe diabetes, and in Cases 8 and 9 the blood sugar was unduly high.

Following this last experience, silk was used uniformly for the closure of the fascia, special consideration was given to the blood sugar in every obese woman, and no further evisceration occurred during the next six months.

It is hard to believe that the simultaneous occurrence of impaired carbohydrate metabolism should be merely accidental in four successive

patients in whom this point was specially considered. In addition there was one patient with glycosuria among the first five, which makes five out of nine cases of wound separation showing the same condition. The regularity of this coincidence makes it probable that diabetes and similar disturbances of the sugar metabolism may interfere with the proper healing of abdominal incisions, and must be considered important causes of wound separation following laparotomy.

Although no further wound separation occurred, there were two cases of secondary infection with unusually widespread abscess formation. As the postoperative course was otherwise uneventful, it was felt that a particularly low tissue resistance must be considered.

In both patients (Cases 10, 11), the inability of the tissue to resist disintegration by a comparatively mild infection was associated with disturbances of carbohydrate metabolism. These two cases seem to explain the common experience that wound infection is more frequent in obese patients. Diabetes and obesity are closely related conditions, and there is some reason to believe that in many cases it is not the obesity itself, but an unrecognized diabetes which must be blamed for the complication.

These two cases with comparatively low resistance to infection may be considered as links connecting the complete wound separation in patients with unrecognized or inefficiently treated diabetes, and their uneventful course, if the disturbance has been controlled by sound management. This contention is supported by the histories of two diabetic patients treated adequately by the Medical Department and transferred for operation (Cases 12, 13).

In both cases the postoperative course was uneventful, and the patients were discharged on the eleventh day following abdominal total hysterectomy. The operations were followed by rises in blood sugar from 126 to 186 mg. and from 155 to 196 mg. per cent respectively, in spite of insulin. This corroborates the observation that physical injury in itself may cause a rise in blood sugar. It is likely that the wound separation in Case 7 (the patient with the severe diabetes) could have been avoided if the operation had been delayed for several weeks and not performed the first day after the blood sugar had dropped from 297 to 175 mg. per cent. Although no ether was used and no glucose was administered following operation, the sudden rise in blood sugar to 241 mg. per cent with its possible detrimental influence on wound healing should have been anticipated.

PROGNOSIS AND DIAGNOSIS

As Table I shows, the mortality following wound separation is appalling though the percentage varies between 12.5 and 72.7 per cent, and certainly depends greatly upon the experience and skill of the surgeon. The poor prognosis is due to the fact that the rupture almost

always occurs unexpectedly and has to be cared for as an emergency. In addition there is no possibility of proper disinfection of the field of operation after the evisceration has taken place. Therefore, early diagnosis, i.e., before the skin has given way, would be of greatest benefit.

TABLE I

AUTHOR	NUMBER OF CASES	RECOVERED	DIED	MORTALITY PER CENT
Madelung, 1905	148	105	43	29.0
				22.3 "purified"
Ries, 1909	6	5	1	16.6
Holtermann, 1925	15	8	7	47.0
Weber, 1926	4	4	–	–
v. Gusnar, 1928	11	3	8	72.7
Horner, 1929	4	1	3	
Sokolov, 1931	725	–	–	32.0 if closed
				35.4 open treatment
Sigalas, 1932	8	–	–	18.5
McCauliff, 1933	3	3	–	–
Meleney, 1934	50	28	22	44.0
Colp, 1934	26	–	–	28.0
Baer and Reis, 1934	7	6	1	14.28
Eliason and McLaughlin, 1934	19	11	8	42.0
v. Graff, 1935	9	8	1	12.5

The accident can occur without any premonitory symptoms following a normal postoperative course, as in three of our patients (Cases 1, 2 and 6). In a fourth patient (Case 5), who was an epileptic and had several severe seizures after operation, diagnosis was impossible. In five of our nine patients, however, the event might have been suspected.

There are two groups of symptoms and signs, the "early" caused by separation of the peritoneum and fascia and incarceration of omentum, resulting in nausea, distention, local pain, vomiting, general malaise and poor appetite; and the "late," i.e., the situation at removal of the skin clips or sutures, when the wound often lacks a healthy appearance (Cases 3, 7) or may be partially separated with the edges devoid of granulations, and probing shows a widespread cavitation under the skin.

Early symptoms were sufficiently developed in three of our patients (Cases 3, 4 and 8) to arouse suspicion. Sugar tolerance tests and blood sugar determinations might have revealed the diabetes and confirmed the suspicion. It might have been possible to save the life of the patient who died (Case 3). In this particular instance there was a bloody serous drainage through a small hole in the upper end of the skin incision, which was indicative of a rupture of the deep layers. Complete evisceration occurred only four days later after skin clips were removed. In two cases (7 and 9) the skin had separated partially, and there was considerable drainage so that evisceration should have been anticipated.

As a whole, the proper evaluation of "early" symptoms is more important because there is sufficient time for the blood sugar determination, which will permit timely recognition of the danger. On the other

hand, anticipation of the evisceration, even by "late" signs, is likely to improve the prognosis, since it allows proper preparation of the patient for the secondary closure.

TREATMENT

Most authors agree that proper treatment consists in secondary closure as soon as eventration has occurred. Eliason and McLaughlin, however, favor tamponage as the less injurious procedure though they have lost four out of five cases in which this method was used. Madelung, Starr and Nason agree that the immediate closure is the proper procedure in noninfected cases, but in the presence of infection recommend tamponage following reposition of the prolapsed intestines. This differentiation is scarcely justified since all cases of evisceration are more or less infected, and experience has taught that the peritoneum is more likely to overcome an infection if the peritoneal cavity is closed.

The final result will always depend upon the general condition of the patient, and the time which has elapsed between evisceration and secondary closure. Therefore, *the essential point is the earliest possible recognition.*

In operations for closure, spinal anesthesia is desirable because of the complete relaxation which facilitates reposition of the intestines. The surrounding skin is wiped with alcohol and ether and painted with merthiolate solution which is less irritating and therefore preferable to tincture of iodine. Omentum and bowel must be carefully mobilized by blunt separation from the edges of the laparotomy wound. No attempt should be made to separate the adhesions which may be found between the loops of bowel or between bowel and omentum. If possible, it is better to close the abdomen in layers, but through-and-through sutures of nonabsorbable material such as silver wire or silkworm-gut should be inserted as additional security. Speed seems to be important and no time should be wasted in an attempt to make an anatomical repair. The healing of the wound following secondary closure is, as a rule, very satisfactory, and our final results have been surprisingly good.

CASE HISTORIES

CASE 1.—S. B., aged sixty years, Hospital No. F 9282. Fibroid of uterus; obesity. Nov. 5, 1931, abdominal total hysterectomy under gas-ether. Uneventful course. Disruption of laparotomy wound on eighth postoperative day. Wound without evidence of infection or healing reaction. Immediate closure. Recovery.

CASE 2.—G. A., aged fifty-three years, Hospital No. E 6532. Cancer of body of uterus; obesity. Aug. 4, 1932, abdominal total hysterectomy under gas-ether. Large amount of glucose intravenously. Uneventful course. Disruption seventh postoperative day following coughing. Conspicuous absence of healing reaction. Immediate closure. Recovery.

CASE 3.—O. S., aged thirty-six years, Hospital No. G 9188. Fibroid of uterus; obesity. Sept. 24, 1932, abdominal total hysterectomy under gas-ether. General

malaise, distention, nausea, serous bloody drainage beginning third day. Disruption suspected, occurred on the seventh day. No healing reaction. Immediate closure. Deceased seventh day following closure. Postmortem: Thrombophlebitis, sepsis, localized peritonitis.

CASE 4.—M. R., aged sixty-four years, Hospital No. H 1772. Twisted pedicle cyst of right ovary; obesity. Feb. 21, 1933, extirpation of cyst and abdominal total hysterectomy under spinal anesthesia. General malaise and depression, distention, nausea, localized pain. Skin clips removed on sixth day; wound appeared unhealthy. Up in chair on eighth day, disruption ninth day. No infection, no healing reaction. Immediate closure. Recovery.

CASE 5.—S. L., aged forty-six years, Hospital No. H 2796. Fibroid uterus; epilepsy. March 23, 1933, abdominal total hysterectomy under gas-ether. Repeated seizures. Removal of skin clips on sixth day, disruption on seventh day following a seizure. Immediate closure. Recovery.

CASE 6.—E. C., aged forty-three years, Hospital No. H 3607. Fibroid of uterus; psychosis. June 22, 1933, abdominal total hysterectomy. Uneventful course. Disruption of laparotomy wound sixth postoperative day. Secondary closure. Blood sugar determinations twenty-two days following disruption revealed a mild diabetes with high renal threshold. Recovery.

CASE 7.—M. E., aged forty-seven years, Hospital No. H 9784. Fibroid of uterus; obesity. Severe diabetes with blood sugar of 297 mg. per cent. Diabetic management before operation. Sept. 15, 1933, abdominal total hysterectomy. Nausea. Skin clips removed sixth day, wound appeared unhealthy. Disruption on the seventh day, the fascia apparently having given way on the second postoperative day. Immediate closure in layers with six through-and-through retention sutures. The accident was probably due to the fact that operation was performed after the blood sugar had been reduced from 297 to 157 mg. per cent for only one day and the diabetes was therefore not fully controlled. The blood sugar rose suddenly following the first and second operations to 241 and 226 mg. per cent respectively, and the poor healing of the wound required considerable increase in the insulin dosage. Recovery.

CASE 8.—M. B., aged fifty-four years, Hospital No. H 8561. Adenocarcinoma of body of uterus; obesity. Deep x-ray treatment. Two months later, Oct. 13, 1933, abdominal total hysterectomy under spinal anesthesia, plus ethylene-ether. Postoperative course unsatisfactory: general malaise, subfebrile temperature, poor fluid intake, nausea, vomiting. On the seventh postoperative day skin clips were removed. Skin was found separated with a piece of omentum in the wound. Immediate closure in layers with additional retention sutures. Sugar++++; blood sugar in spite of diabetic management 159 mg. per cent three weeks after operation. Recovery.

CASE 9.—H. F., aged fifty-nine years, Hospital No. H 13782. Postmenopausal bleeding; obesity. Dec. 16, 1933, abdominal total hysterectomy under spinal anesthesia. Sixth day skin clips removed. Skin partially separated with profuse discharge of bloody serum. Disruption suspected, but recognized only on the fourteenth day. Immediate closure in layers. Sugar++; blood sugar 155 mg. per cent. Recovery.

CASE 10.—M. B., aged fifty years, Hospital No. J 5543. Cancer of cervix, Schmitz II, fibroid of uterus and obesity. May 31, 1934, abdominal radical operation (Wertheim) under spinal anesthesia. Postoperative course: moderately febrile, but otherwise uneventful. On the seventh day a fluctuating abscess developed, which was evacuated by blunt separation of the skin incision in its full length. The sutures of the fascia seemed to be intact. Blood chemistry revealed a blood sugar

of 138 mg. per cent, and antidiabetic regime was started. The infection cleared up readily and the patient was discharged with an almost healed wound on the sixteenth postoperative day.

CASE 11.—M. H., aged thirty-nine years, Hospital No. J 5702. Peritoneal adhesions; cystocele; cervicitis. May 28, 1934, abdominal total hysterectomy. Postoperative course: uneventful except for moderate fever for three days. The patient was allowed up on the eighth postoperative day. The following day a small draining sinus was found near the upper end of the incision through which great quantities of pus had been emptied. On the eleventh day probing gave evidence that the skin in the entire length of the incision was undermined and had to be opened to its full extent. At this time the silk sutures of the fascia were intact except for a few centimeters at the lower end. Secondary closure. The peritoneum was firmly healed and no evisceration had taken place. A sugar tolerance test which had been made the day the draining sinus was discovered gave the following results:

Hours	0.0	0.5	1.0	1.5	2.0	2.5
Bl. sugar	124	179	231	231	212	
Urine sugar	0		0		0	

Blood sugar the second day following closure was 186 mg. per cent. The patient was therefore considered as a diabetic with high renal threshold and was put under antidiabetic management. Further course was uneventful.

CASE 12.—G. W., aged fifty-six years, Hospital No. H 4145. Diabetes; adenocarcinoma of body of uterus. Blood sugar prior to operation 126 mg. per cent. Abdominal total hysterectomy under spinal anesthesia without additional gas or ether. Blood sugar 165 and 186 mg. per cent on the days following operation. Uneventful postoperative course. Discharged on the eleventh day.

CASE 13.—B. C., aged thirty-eight years, Hospital No. H 6681. Diabetes; fibroid of uterus; chronic appendicitis. Blood sugar prior to operation 155 mg. per cent. Abdominal total hysterectomy under ethylene-ether. Blood sugar 196 and 170 mg. the days following operation. Uneventful postoperative course. Discharged on eleventh day.

SUMMARY

1. Nine cases of wound separation following laparotomy are reported.

2. All but one patient recovered following *immediate closure.*

3. Blood sugar determinations and sugar tolerance tests performed in four successive cases revealed a diabetic condition.

4. Disturbances of carbohydrate metabolism are believed to be an important cause of postoperative separation of abdominal incisions.

5. Considering the high coincidence of obesity and diabetes, stout patients should have blood sugar determinations before laparotomy.

6. Because of its unlimited tensile strength, nonabsorbable material is recommended for the closure of the fascia to safeguard the wound in cases of retarded healing.

7. Recognition before evisceration actually occurs is possible in many cases and improves the final results.

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DISCUSSION

DR. EARL C. SAGE, OMAHA, NEB.—The new viewpoint that "disturbance of the carbohydrate metabolism is an important, if not the only, cause of postoperative separation of abdominal incisions," is worthy of consideration. Personally, I would not take such a decided stand, as I believe that there are other predisposing and exciting causes.

We can say that the *predisposing causes* of disruption of abdominal wounds are senility, decrepitude, malignancy, jaundice and a peculiar body tissue function that dissolves catgut earlier than usual. As Dr. von Graff has pointed out, the diabetic state should also be included here. The exciting causes are constant coughing, hiccoughing, sneezing, distention, undue abdominal strain, and infection.

Kennedy, drawing on the combined surgical experiences of himself and Joseph Price, during fifty-six years, reported that not a single disruption of an abdominal wound occurred with the use of through-and-through silkworm-gut sutures. He recommended the omission of all absorbable sutures, especially in the closure of wounds in layers. There is the equally impressive statement by Baldwin, that he performed 16,465 laparotomies without a dehiscence using No. 2 chromic catgut throughout in the closure of the layers of peritoneum, muscle, fascia and skin, and silkworm-gut for stay sutures. He particularly emphasized the use of the binder throughout the postoperative period and convalescence. As a contrast is the report of Sokolov, who, in 1932, collected and reviewed 730 cases of wound rupture after laparotomy and concludes from 1,000 questionnaires sent to surgeons in Europe that disruption of the abdominal wound takes place in 2 to 3 per cent of abdominal operations.

The traction force of any kind of absorbable material is of short duration. It loses its tensile strength long before it is absorbed. Howes, in the experimental department of Yale University, finds that chromic twenty-day No. 1, with a normal strength of twelve pounds, in twelve hours has a strength of six pounds, in twenty-four hours of two and one-half pounds, in thirty-six hours, 0. The holding strength of a stitch in fascia varies from seven to eight and one-half pounds. The holding strength of a strand of No. 0 catgut is nine pounds; thus, before a strand of catgut will break, it will tear through the tissue.

Baldwin has furthermore reviewed the experience of five surgeons in New York City as given in their papers at the November, 1933, meeting of the New York Surgical Society, where they admitted that by their technics they average one, two, or even three disruptions, with exposure or extrusion of abdominal contents, in every 100 abdominal operations. In none of the hospitals from which their reports came were retention sutures a routine measure.

It is my impression from studying the literature, that the routine use of stay or retention sutures, not removed before the tenth or twelfth postoperative day, and the use of properly adjusted adhesive straps and supporting abdominal binders would greatly reduce the incidence of postoperative disruption of abdominal wounds and hernias.

DR. FRED J. TAUSSIG, ST. LOUIS, MO.—One of the predisposing factors that I personally consider most important in our experience at the Barnard Free Skin and Cancer Hospital is anemia. In suturing the abdominal incision, I would particularly stress that after making a midline incision through the skin we do not also make a midline incision through the fascia.

I prefer to use No. 2 twenty-day catgut both for peritoneum and fascia and also employ a through-and-through fish-line tension suture which is not removed until approximately the tenth day. I would hesitate very much to use silk for the fascia because of experience in infected cases where such silk knots act as a foreign body and take months to come out through the wound. We should realize that the wound is weakest at about the eighth or ninth day, and at this time when we change our dressing we should not be content with a small strip of adhesive but use a wide strip for the next four days, so that the abdominal incision is thoroughly supported.

DR. JACOB L. DUBIS, CLEVELAND, O.—The type of incision that I have used for years with good satisfaction is the Pfannenstiel. One can take out a tumor up to the umbilicus with this incision. There is less wound infection and the use of the silkworm-gut is unnecessary. Overlapping the fascia gives added strength. Important points in the technic are the stopping of all bleeding and oozing, and the careful avoidance of traumatism.

DR. CARL HENRY DAVIS, MILWAUKEE, WIS.—Most of us will agree also that a large proportion of wound difficulties are not wound infections primarily, but they are cases where hemostasis was not perfect, serum collected, causing separation of the tissues with imperfect healing.

DR. FRED H. FALLS, CHICAGO, ILL.—Usually a day or two days before the actual evisceration there occurs a leakage of serum from the wound. Whether that occurs because of the failure of proper hemostasis in the wound edges or whether the serum comes from the peritoneal cavity and precedes the actual separation, I do not know. Whenever we see our dressings wet with serum we presume that evisceration is already present and take steps to prevent an actual extrusion of the bowel.

Second, evisceration is apt to occur in women with asthma where the wound is continually being put under tension due to the labored breathing. In two cases of this kind in my experience loops of bowel were left outside of the abdomen for several days until the dyspnea improved. Both patients recovered after the delayed return of the bowel to the peritoneum.

DR. JEAN PAUL PRATT, DETROIT, MICH.—Wound healing takes place by formation of capillary loops, that is, granulation tissue. General conditions which interfere with the proper blood supply, such as debilitating diseases, undernutrition or starvation, affect the nutrition of the tissues involved in wound healing and cause delayed repair. Tension from stay sutures has seemed to us a local factor impairing circulation. In a comparative series of cases our results have been better without stay sutures. Heavy catgut affords more foreign body to be carried away and therefore interferes with wound healing, and it has been our practice to use catgut not heavier than No. 1 for wound closure.

DR. VON GRAFF (closing).—When silk or stay sutures are used, they may, in spite of impaired healing, minimize the incidence of disrupture by holding the tissue sufficiently long in contact. During this period, the patient may overcome any temporary impairment of the sugar metabolism.

We occasionally see the very rapid development of incisional hernias. The fascia is always found separated but the subcutaneous tissues and skin have healed, thus preventing evisceration. If there had been an impairment of the healing tendency, such as in diabetes, the separation would have involved, not only the fascia, but the rest of the abdominal wall.

HORMONAL STUDIES WITH THE OVIPOSITOR LENGTHENING REACTION OF THE JAPANESE BITTERLING*

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IN A preliminary report[1] the authors demonstrated what was believed to be a biologic test for the estrogenic hormone present in excessive amounts in the urine from pregnant women. As was feared, it was immediately assumed by many of our readers that we were advocating a new biologic test for pregnancy and because of such misinterpretation the caution that was exercised in avoiding definite conclusions was apparently unavailing. From our further studies as well as the published work of Szusz,[2] Fleischmann and Kann,[3] and Ehrhardt and Kuhn,[4] estrogenic substance is fairly firmly established as the exciting factor in the production of the phenomenon that constitutes the criterion for the test. For this work the Japanese bitterling *(Acherlognathus intermedium)* was used because the female of this fish has an ovipositor which is always visible to the naked eye. Only fish that had been standardized according to the technic we have described were used. Our reports are the only ones in which such standardized fish had been used exclusively. As our studies progressed, it became more and more apparent that the bitterlings, like any other animals used for checked investigative work, must be put through a standardization process before results could be comprehensively evaluated. The process is simple and the mortality among the fish is less than 2 per cent. The work of Kotz, Douglas and Parker[5] illustrates this point. We have experienced no particular difficulty in keeping the fish alive in our tanks and through a large series of often repeated tests, except at one time when a supply of the German bitterlings (*Rhodeus amarus*) introduced a fatal fungous infection.

Normally, during the breeding season (April 15 to July 1), and in the presence of the male, the ovipositor elongates from its latent 2 to 4 mm.

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to a distance of 15 to 25 mm. If the female bitterlings are segregated from the males this natural lengthening process does not occur. It was found that by stimulation with the estrogenic hormone it is possible, artificially, to reproduce the ovipositor lengthening during any season of the year and not, as Szusz thought, only during the breeding season. It was also found that the fish reacted in a satisfactory manner when the hormone was dissolved or suspended in the water they inhabit, making it unnecessary to inject the products into the fish as did Fleischmann and Kann, thus reducing the chances of injuring or killing the test animal. By applying these principles we use the same fish for repeated tests allowing a recovery period of two to three weeks for the elongated ovipositor to return to its normal state before a further test is attempted.

The fish are placed in a liter of fresh water containing 4 c.c. of the urine to be tested. Observations are made at twenty-four-hour intervals for a period of seventy-two hours. Should the ovipositor extend well beyond the margin of the ventral fin, the test is considered as being positive. In the event that the ovipositor reaches just to the fin margin or above this, the test is read as being negative. The actual length of the extension of the ovipositor beyond the fin margin is of no apparent significance. Ehrhardt and Kuhn rate their tests, and thus the materials tested as +, ++, and +++ according to the distance beyond the fin margin that the elongated ovipositor attains. Kotz, Douglas and Parker mention "moderately positive" tests. We have felt this to be an unreliable method of designation for either the potency of the product tested or the estrogenic hormone content of the urine. This is a logical conclusion for us to reach when, during the course of our standardizations, we have repeatedly obtained all stages of ovipositor lengthening as a result of stimulation on several fish by a single urine specimen. Suffice it to say that an ovipositor lengthening beyond the fin margin is a positive reaction.

At this time it seems advisable to strengthen our contention that the reaction here discussed is a product of stimulation by estrogenic substance. An exhaustive study of the gross and histologic anatomy of the bitterlings both in their normal state and when artificially stimulated has aided us somewhat in this deduction. The ovipositor has the histology of the human cervix uteri. Under stimulation there is a dilatation of the lumen, the blood vessels and the lymphatic spaces, with occasional pigmentation but no actual cellular changes. The ovary and oviduct are unaffected by the artificial stimulants. If we may be allowed to draw analogies between the fish and the mammals we see the same thing in the mouse, the rat, and the rabbit under estrogenic hormone stimulation, changes in the cervix and vagina with no noticeable effect upon the ovaries.

To enhance this view we destroyed the gonadotropic hormones in urine by boiling and the subsequent tests were all positive. To prove this point to our entire satisfaction we proceeded to test pure hormonal, commercial hormonal, and gland extract products. In order to carry out this work we appealed to Dr. E. A. Doisy who very graciously supplied us with

generous samples of his purified estrogenic substances theelin, theelol, and dihydrotheelin in 0.05 NaOH solution. We wish, at this time, to express our most sincere thanks to Dr. Doisy for his willing cooperation. Tables I and II show the results of this work, the interesting features of

TABLE I. OVIPOSITOR LENGTHENING REACTIONS OBTAINED WITH VARIOUS HORMONAL PRODUCTS

PRODUCT	AMOUNT	REACTION					
		24 HR.	48 HR.	72 HR.	96 HR.	120 HR.	2 WK.
Theelin	100 R.U.	Neg.	Pos.	Pos.			
Parke, Davis Co.	150 R.U.	Neg.	Pos.	Pos.			
	300 R.U.	Neg.	Pos.	Pos.			
Progynon Tablet	22½ R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Schering	45 R.U.	Pos.	Pos.				
Ether extract of	45 R.U.	Pos.	Pos.				
Ether residue of	45 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
	1 c.c.	Pos.	Pos.	Pos.			
Emmenin	1 c.c.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Ayerst, McKenna and	2 c.c.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Harrison	3 c.c.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Ether washed	4 c.c.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Amniotin	50 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Squibb	150 R.U.	Pos.	Pos.	Pos.			
Suppository	1	Pos.	Pos.	Pos.			
Theelin	100 R.U.	Neg.	Neg.	Neg.	Neg.	Pos.	Pos.
Doisy	200 R.U.	Neg.	Neg.	Neg.	Neg.	Pos.	Pos.
	300 R.U.	Neg.	Neg.	Neg.	Pos.	Pos.	Pos.
	400 R.U.	Neg.	Neg.	Neg.	Pos.	Pos.	Pos.
Theelol	5 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Pos.
Doisy	10 R.U.	Neg.	Neg.	Neg.	Neg.	Pos.	Pos.
	15 R.U.	Neg.	Neg.	Neg.	Pos.	Pos.	Pos.
	20 R.U.	Neg.	Neg.	Neg.	Pos.	Pos.	Pos.
Dihydrotheelin	825 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Pos.
Doisy	1,650 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Pos.
	2,067 R.U.	Neg.	Neg.	Neg.	Neg.	Pos.	Pos.
	2,475 R.U.	Neg.	Neg.	Neg.	Neg.	Pos.	Pos.
Pregnancy urine	4 c.c.	Pos.	Pos.	Pos.			
Ether extract of	4 c.c.	Pos.	Pos.	Pos.			
Ether residue of	4 c.c.	Neg.	Neg.	Neg.	Neg.	Neg.	
Antophysin	1,000 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	
Winthrop							
APL							
Ayerst, McKenna and	1,000 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	
Harrison							
Antuitrin-S							
Parke, Davis Co.	1,000 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Pure Prolan							
Dr. Lawrence	1,000 R.U.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Univ. of Chicago							

these being the delayed positive reactions obtained with the purer estrogenic substances as compared to the more rapid results evidenced on testing with the unerystallized commercial products (progynon, amniotin,

TABLE II. REACTIONS USING VARIOUS GLAND EXTRACT PRODUCTS

SUBSTANCE	AMOUNT	REACTION 24 HR.	48 HR.	72 HR.	96 HR.	120 HR.
Parathyroid	⅗ gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Adrenal	3 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Spleen	4 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Testis	4 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Placenta—desiccated	6 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Pancreas	6 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Mammary gland	5 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Thyroid	5 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Pineal	⅕ gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Bone marrow	5 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Prostate	6 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Thymus	6 gr.	Neg.	Neg.	Neg.	Neg.	Neg.
Antuitrin-G	80 units	Neg.	Neg.	Neg.	Neg.	Neg.

emmenin). We also find that ether extracts of these products and of pregnancy urine remove the estrogenic principles, the ether extract giving positive results while the residues produce constant negatives. This phase of our work strengthens our conviction that an estrogenic principle produces the ovipositor lengthening reaction. Negative results were obtained at all times on the gland extract products as well as on all the gonadotropic hormone products tested. We believe that in the crystallization process, changes take place in the estrogenic products that decrease the efficiency of their action upon the ovipositor of the bitterling.

Ehrhardt and Kuhn claim the reaction to be one of a specific hormone for ovipositor lengthening (legerohrenhormon) which is so closely related to the estrogenic hormone in action that the two may be isomers. They drew this conclusion when unsatisfactory results were obtained by use of urine from pregnant mares, a urine known to contain a tremendous amount of estrogenic substance. According to Doisy[6] the estrogenic substance obtained from the mare's urine is not the same as that derived from the urine of human beings. This fact, together with the delayed reactions obtained from the pure hormones of Doisy, detracts considerably from the main evidence in favor of the theory of Ehrhardt and Kuhn.

In a more recent article Baumann and Szusz[7] reach a conclusion similar to that of Ehrhardt and Kuhn, claiming the ovipositor lengthening function to be the action of a specific hormone which they designate as the "harnfraktion." These authors do not give their method of extraction of this fraction from the urine, but they claim the action of their specific hormone is partly that of prolan and partly that of estrin while being specifically neither of these. They obtained thecalization in the ovaries of adult rats with the production of atretic corpora lutea and an excess production of theca lutein cells without the formation of follicles, while they demonstrate no typical reaction on the ovaries of infantile rats. We are not familiar, either from personal experience or from a study of the literature, with any single hormone that has a gonadotropic and estrogenic function such as is claimed in this instance by Baumann and Szusz. Until we are made aware of the method of production of the "harnfraktion" we must assume that Baumann and Szusz were dealing with a product contaminated by prolan which in our work has not had the least effect upon the ovipositor of the bitterling.

Fleischmann and Kann[8] have recently published another report in which they state that the estrogenic hormone is the activating principle in the production of ovipositor lengthening. Their evidence is very similar to that which we have presented in Tables I and II.

We must again preface our presentation with a warning against misinterpretation of the type that led Kleiner, Weisman, and Barowsky[9] to publish their report. Aschheim[10] states that very early in pregnancy there is an increase in the amount of anterior pituitary-like gonadotropic hormone in the urine which reaches a maximum early and maintains this throughout the life of the pregnancy, while the urinary estrogenic hormone content reaches a demonstrable level at about the midpoint in the pregnancy and increases greatly in amount from this time to the end of gestation. Further, he brings out that with the death of the pregnancy the gonadotropic hormone excesses are quickly dissipated. In our work, urine from patients in which the gonadotropic hormone excesses have proved to be dissipated, contains estrogenic hormone in sufficient quantity to give a positive test upon the fish. It is because of such evidence that we might expect a test dependent upon the estrogenic hormone to be of less value in the detection of very early pregnancy than those tests dependent upon the gonadotropic hormone for their efficiency (Aschheim-Zondek and Friedman tests). Conversely, a test for excesses in estrogenic hormone would prove more valuable as a diagnostic aid in conditions where the pregnancy is dead.

Because of the relative simplicity of procuring and segregating suitable animals and because of the decreased technical difficulties, most of the laboratories with which we are familiar have substituted the Friedman test for the Aschheim-Zondek test. In an attempt to evaluate the possibilities of the test upon the bitterling as a pregnancy test we ran 132 consecutive specimens of urine parallel to Friedman tests. In this series, cases for diagnosis in the routine conduct of several gynecologic and obstetric services were used; the results not included in this report being those in which the two tests were at variance and no final diagnosis was available. Table III shows the result of this study. The tests agreed in 84.4 per cent of the cases; the other 14.6 per cent are analyzed below.

1. Ectopic pregnancy, ruptured. Proved at operation. Test upon fish positive. Friedman test negative.

2. Intrauterine pregnancy of four months' duration. Very obese woman with malignant hypertension. Bimanual examination unsatisfactory. Test upon fish positive. Five rabbits killed by toxicity of urine. Friedman test negative.

3. Early intrauterine pregnancy seven days after the date of the first missed period. Proved by subsequent development of the pregnancy. Test upon fish positive. Friedman test negative. Subsequent Friedman test positive.

4. Missed abortion. Seven months' amenorrhea with uterus enlarged to the size of a six to eight weeks' pregnancy. Material recovered at curettage showed retained and organized placental tissue with chorionic villi. Test upon fish positive. Friedman test negative.

5. Placental polyp. Continuous bleeding for five months following spontaneous delivery at term. Curettage revealed a polyp which was made up of placental tissue with chorionic villi. Test upon fish positive. Friedman test negative.

6. Ectopic pregnancy. Proved at operation. Test upon fish positive. Friedman test negative.

TABLE III. TEST UPON THE BITTERLING IN PREGNANCY. ONE HUNDRED THIRTY-TWO CONSECUTIVE TESTS CHECKED AGAINST THE FRIEDMAN TEST

Positive to both tests	51
Negative to both tests	62
Positive fish—negative Friedman test	15
Negative fish—positive Friedman test	4
Total tests	132
Disagreements	19
Per cent disagreements	14.4%

ERRORS

	FISH IN ERROR	FRIEDMAN IN ERROR
Early pregnancy	2	2
Ectopic pregnancy	0	5
Endocrine disorder	0	1
Salpingitis	2	0
Pregnancy toxemia	0	1
Incomplete abortion	1	2
Menopause	1	0
Missed abortion	0	1
Placental polyp	0	1
Errors	6	13
Per cent errors	4.5%	9.8%

7. Incomplete abortion, eight weeks' duration. Proved at operation and on microscopic section. Test upon fish positive. Friedman test negative.

8. Subacute salpingitis. Suspect ectopic pregnancy. Proved by posterior colpotomy. Test upon fish positive. Friedman test negative.

9. Ectopic pregnancy. Proved at operation. Test upon fish positive. Friedman test negative.

10. Early pregnancy, intrauterine; five days after first missed period. Test upon fish negative. Friedman test positive. Subsequent fish test positive.

11. Early pregnancy; seven days after first missed period. Test upon fish negative. Friedman test positive. Test upon fish one week later positive.

12. Menopause. Patient amenorrheic for two months. Menstruated shortly after tests were run. Test upon fish positive. Friedman test negative.

13. Ectopic pregnancy. Proved at operation. Test upon fish positive. Friedman test negative.

14. Periods of amenorrhea alternating with menometrorrhagia. Curettage revealed pseudopregnancy reaction of endocrine dysfunction. Test upon fish negative. Friedman test positive.

15. Early pregnancy; four days after first missed period. Test upon fish positive. Friedman test negative. Friedman test five days later positive.

16. Subacute salpingitis. Proved at operation. Test upon fish positive. Friedman test negative.

17. Ectopic pregnancy. Proved at operation. Test upon fish positive. Friedman test negative.

18. Incomplete abortion. Proved on curettage and microscopic examination. Test upon fish negative. Friedman test positive.

19. Incomplete abortion. Proved on curettage and microscopic examination. Test upon fish positive. Friedman test negative.

The results of these tests bear out what was shown in the last paragraph, that the errors in any test dependent upon the estrogenic hormone are likely to be most marked in cases of early pregnancy, while errors in tests using the gonadotropic hormone as their bases are most frequent in cases in which the ovum has died (ectopic pregnancy, incomplete abortion, missed abortion, placental polyp). These findings are in accord with those of Goldberger, Salmon, and Frank[11] who reported 32 per cent false negative Friedman tests in a series of ectopic pregnancies.

In twenty cases followed throughout the puerperal period by testing the urine every other day it has been established that the positive test upon the urine disappears rather early. All tests were negative by the eighth postpartum day, while eight of the twenty had negative tests on the fourth day.

Table IV lists a group of forty student nurses on whose urines tests were done. The only information obtained from these girls was the date of the last menstrual period. Menstrual abnormalities, state of general health, existence of gynecologic pathology, and possibilities of endocrine derangement of one type or another were not divulged and thus the possibility for error seems great. From the results of these tests it can be seen that positive results may be obtained on the urines from nonpreg-

TABLE IV. TESTS UPON URINES FROM 40 NONPREGNANT FEMALES

DAYS FROM LAST MENSTRUATION	POSITIVE	NEGATIVE
2		1
3	1	
4	1	
6		1
8	2	
9	1	1
10	1	1
11	1	
12	1	1
14	2	2
15	1	
16	1	1
17		1
19	1	1
20	1	
22	1	1
23		2
24	1	1
25	1	
26	3	1
32	2	
33	1	
34		1
40		1
Totals	23	17

nant women at various and varying times during the menstrual cycle. Because this is at variance with the work of Frank[12] on the levels of the female sex hormone in the blood and urine during the course of a menstrual cycle we are, at the present time, at a loss to explain such results. Were these forty women examined physically and were their histories closely inquired into, we might be able to reach some conclusions.

Two women who have regularly recurring menstruation and who lack any pelvic abnormalities were followed throughout two consecutive menstrual cycles by testing urines at three-day intervals. In both negative tests were obtained at all times except at mid-menstruum, the time of ovulation. Frank found this to be the time when the estrogenic hormone content of the urine and blood was at its cyclic maximum.

In an attempt to determine the possibility of transmission of the excesses in estrogenic hormone at term from the mother to the fetus, the urines of fifteen newborn infants were tested. In only one instance, a female child four days old, was a positive test obtained, all others giving negatives (Table V).

TABLE V. TESTS UPON URINES FROM NEWBORNS

AGE	SEX	REACTION
4 days	F	Pos.
7 days	F	Neg.
10 days	M	Neg.
6 days	F	Neg.
10 days	M	Neg.
6 days	M	Neg.
6 days	M	Neg.
5 days	M	Neg.
4 days	F	Neg.
3 days	F	Neg.
9 days	F	Neg.
14 days	F	Neg.
6 days	M	Neg.
7 days	F	Neg.
5 days	F	Neg.

Heckel[13] has been pursuing the work upon the bitterling from the urologic standpoint and up to the present time he has a number of tests upon the male. He has been kind enough to allow us to use some of his results in this paper. Heckel has found that normal adult male urine gives positive tests using the technic that we have described, but if the amount of urine is decreased the tests become negative. He found that 2 c.c. of urine is the ideal amount for testing purposes as this gave consistently negative results in normal adult males. Boiling of the urine did not destroy the active principle in the production of the test. In six male patients with testicular atrophy based upon a previous parotitis, the tests were all negative even when using 4 c.c. of urine. In three male patients with testicular tumors (one teratoma, one chorionepithelioma, and one of undetermined origin), the tests were all positive on using 2 c.c. of urine. More details of this work will be available when Heckel makes his formal reports.

In testing the urines of several boys between the ages of seven and ten, it was found that the tests were negative as were those on several girls under ten. This is interesting so far as it suggests further problems, mainly the testing of urines

of boys approaching the age of puberty in order to determine at what age the exciting hormone makes its appearance in amounts that can be demonstrated and possibly gives us a means of predicting the onset of puberty.

Five patients with benign lesions of the breast (cystic mastitis) submitted urine for testing and all gave positive results. One of these is particularly interesting because this patient has had a five-year amenorrhea associated with the mammary gland hyperplasia. This is understandable when we see amenorrhea associated with the presence of theca and granulosa cell tumors of the ovary apparently based upon the production of excessive amounts of estrogenic hormone by these tumors.[14] In line with this, it is of interest at this point to note that a portion of theca cell tumor weighing 1.9 gm. was extracted with ether and the extract used for testing; the test upon the bitterling was positive after forty-eight hours.

DISCUSSION

The test for estrogenic hormone using the ovipositor lengthening function of the Japanese bitterling as the criterion has proved to be of value in detecting excesses of the hormone in the urine of females associated with pregnancy, endocrine disturbances, and chronic cystic mastitis. In expecting consistent results with the minimum of error or misinterpretation we urge that only fish which had been previously standardized be used for testing. This is an extremely important factor that has been repeatedly impressed upon us in the conduct of some 1,000 tests. Without such a standardization negative tests are of no significance because we are not certain about the reactability of the fish until we have proved that it is not refractile to the estrogenic hormone as contained in urine.

In testing with commercial hormonal products it was found that estrogenic preparations gave uniformly positive results, the amount of hormone in rat units necessary to produce a positive test varying with the various products. In all instances, preparations of the gonadotropic hormone gave negative results. Because of the many factors involved in such a study we can make no statement nor can we draw any definite conclusions as to the potency of the products tested. Variations in solubility, ingestibility, pH, purity of estrogenic substance, and side action of the "fillers" or vehicles possibly acting as factors affecting the speed or efficiency of the product in causing ovipositor elongation.

In attempting to use this reaction as a test for pregnancy, several precautions are advisedly given. It must be remembered that we do not advocate replacement of the Aschheim-Zondek or Friedman tests by this test for the diagnosis of early pregnancy because of the biologic facts that tend to show that the gonadotropic hormone excesses associated with pregnancy appear earlier than do the estrogenic principles. In our series there were two early pregnancy tests that were Friedman positive and fish negative and two that showed just the opposite findings. This is possibly explained by the fact that although the gonadotropic hormone excesses appear earlier, they do not reach a sufficient concentration in the urine to give the Type II and Type III reactions of Aschheim but merely show the follicle formation he designates as Type I reaction and which is not construed as a definite positive. On the other hand, although the

estrogenic hormone increase is not rapid, it may be possible that the ovipositor lengthening function demands less concentration for detection than does the Allen-Doisy method of testing for this hormone. At any rate, we have demonstrated in our tests parallel to Friedman tests that in cases where the ovum is dead the test dependent upon the estrogenic hormone has more value than does one which utilizes the gonadotropic hormone. We feel that in conjunction with one of the other biologic tests, the test upon the bitterling will prove of value as an aid in diagnosis where ectopic pregnancy, incomplete abortion, missed abortion, placental polyp, or any other condition where the death of the fetus is suspected. In fairness to the test may we urge that it not be used indiscriminately on unknown urine as a test for pregnancy but rather that it be considered an aid in diagnosis in such cases where the history, physical and pelvic findings, and one of the other biologic tests have failed to coordinate, and further substantiation is advisable. Only when we are familiar with all the facts in any clinical problem can we apply the test as a diagnostic aid in pregnancy conditions.

We are now engaged in checking the work that is embodied in this and our previous report as well as upon new problems in this field. In our future studies we shall attempt to determine, by studies on the blood and urine of normally menstruating women, just what concentration of estrogenic hormone is necessary to produce a positive test and possibly show that we are dealing with a biologic reaction which is more sensitive to that hormone than are the other methods now available.

In conclusion, our work shows that only those preparations containing estrogenic substance can influence ovipositor lengthening. Pregnancy urine, urine from nonpregnant women at certain stages in the menstrual cycle, urine from sexually active males, urine from women with cystic mastitis, and extracts of some tumors give positive tests. We also must conclude that the activating hormone is heat stabile, and apparently ether soluble.

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DISCUSSION

DR. ERWIN von GRAFF, DES MOINES, IOWA.—We may expect a positive pregnancy test only in the presence of living and functioning placental tissue. In many cases of incomplete abortion and ectopic pregnancy, the test may be negative because the placenta has been separated.

In one of his charts, Dr. Bauer has cited, as failures, a number of cases of ectopic and incomplete abortion in which the bitterling test was negative. I do not agree that the test failed. The fault lay in the evaluation of the result, as a positive test was not to be expected.

DR. H. CLOSE HESSELTINE, CHICAGO, ILL.—I would like to ask some questions. First, were the extracts used for the test from male or female subjects and were the sources human? If from females, were the females pregnant? Second, what effect does drying have upon the estrogenic hormone?

DR. BAUER (closing).—The desiccated placental extracts on the market do not give positive tests, while those prepared according to Dr. Collip's method do have some effect. I cannot say whether the extracts were made from the human being or from animal material, as they were all proprietary extracts.

While we could not expect Friedman's test to be positive where the fetus has been dead for some time, it simply brings out the point that the value of the Friedman test in these conditions is not as great as we heretofore supposed. We think the bitterling test has a value which the Friedman test does not. This test is not one that can be used as a standardization process to determine a definite number of rat units. It simply tells us whether we have estrogenic hormone. If we get a positive test we have an amount of estrogenic substance comparable with that found in the urine of pregnant women at or near term.

Soimaru, A.: Generalized Peritonitis From Rupture of a Pyosalpinx, Gynécologie 34: 21, 1935.

Generalized peritonitis following rupture of a pyosalpinx is third in frequency in the causes of general peritonitis. The first two causes are appendicitis and gastroduodenal complications. In the author's clinic, among 179 instances of pyosalpinx there were 5 ruptures into the free peritoneal cavity, an incidence of 2.8 per cent. The ruptures are usually due to trauma or are spontaneous perforations. In the former instance the liquid forced into the peritoneal cavity is not necessarily virulent whereas in the latter it always is highly virulent. A rupture may be produced during a rough gynecologic examination, it may follow manual or instrumental manipulations on the cervix, efforts to produce abortion, unusual efforts on the part of the patient such as lifting heavy weights, after a fall, and after strenuous exercise. At the moment of rupture there is sudden intense pain followed by disappearance of the pyosalpinx. This is usually followed by tenseness of the abdominal wall. Vaginal examination will reveal exquisite tenderness of the culdesac of Douglas without the presence of a mass.

The prognosis depends upon the time of intervention, the general condition of the patient, and the simplicity of the operation. The mortality has decreased in recent years from 70 per cent to 7.6 per cent. The treatment consists of immediate operation. The author believes that simple colopotomy followed by vaginal drainage is insufficient and illogical. Likewise mere abdominovaginal drainage does not give the good results. He believes that the best treatment consists in the removal of tube and ovary followed by drainage with a Mickulicz sac. Four out of his five cases were cured by this procedure.

J. P. GREENHILL.

MECHANICS OF UTERINE SUPPORT AND POSITION*

I. Factors Influencing Uterine Support (An Experimental Study)

William F. Mengert, M.D., Iowa City, Ia.

(From the Department of Obstetrics and Gynecology, State University of Iowa)

SO MANY theories are current concerning the mechanism of uterine support that it seemed worth while to attempt a quantitative evaluation of the relative importance of every possible means by which the uterus may be retained in the pelvis. The method employed, namely, traction on the uterus of a cadaver, was used in 1858 by Legendre and Bastien.[6]

MATERIAL AND METHOD

The material comprised eight cadavers. Table I shows the age at time of death, the interval which elapsed between death and the experiment, and gives detailed data concerning each subject. All of the subjects were in states of normal nutrition at the time of death, and the pelvic organs were normal to inspection. There were no evidences of prolapse of the uterus or vaginal walls.

Each body lay supine in the usual position for postmortem examination. After the abdomen had been opened by the usual midline incision, a tenaculum was placed on each lip of the cervix and a string bearing a 1 kg. weight was passed over a pulley at the foot of the table and attached to the tenacula. The uterus was thus subjected constantly to the traction of 1 kg. exerted in the long axis of the body. A meter bar was laid on the table between the legs of the cadaver, parallel to the course of the string from cervix to pulley, and a convenient point to serve as a marker was chosen on the string. By observing the relation of this point to the meter bar it was possible to measure accurately the descent of the uterus as successive structures were severed.

The distance from cervix to introitus was measured and recorded at the beginning of each experiment (Table I).

The paired structures attached to the uterus were then severed in varying sequences. For the purposes of this study eight pairs of structures were recognized, as follows: (1) round ligaments, (2) ovarian and infundibulopelvic ligaments, (3) upper third of the broad ligaments, (4) lower two-thirds of the broad ligaments, (5) upper third of the paravaginal tissues, (6) middle third of the paravaginal tissues, (7) uterosacral, and (8) pubocervical ligaments. In addition, the pelvic floor musculature was considered as a possible support of the uterus. In two subjects (Nos. 6 and 8) the vagina was detached from the cervix by circumcision early in the experiment. Obviously, this procedure eliminated the paravaginal tissues from consideration in these two subjects.

RESULTS

The descent of the uterus following section of each pair of structures is recorded in Table II. It will be seen that division of the round, ovarian, infundibulo-

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

The second paper of this series will be published in the June issue.

TABLE I. DATA ON SUBJECTS*

Subjects arranged in the chronologic order in which they were obtained. Note that the uterus did not descend below the introitus in a single subject before the beginning of an experiment. Hence, there were no cases of preexisting prolapse.

IDENTIFICATION	HOSPITAL NUMBER	AGE	PARITY	HEIGHT (CM.)	DISEASE CAUSING DEATH	TIME ELAPSED BETWEEN DEATH AND EXPERIMENT	RIGOR MORTIS	PROLAPSE PRODUCED BY ONE KILOGRAM TRACTION (RELATION TO INTROITUS)
1. F. H.	K 4495	27	2	164	Septicemia following wound of foot	2 hr. 40 min.	0	2 cm. plus
2. N. B.	K 5687	53	5	166	Cardiac failure	4 hr. 45 min.	0	0
3. C. H.	K 8081	51	5	160	Stenosis common bile duct. Postoperative pneumonia	4 hr. 30 min.	4-plus	2 cm. plus
4. I. A.	K 8026	47	7	157	Bronchopneumonia	5 hr. 25 min.	1-plus	1 cm. plus
5. M. J.	K 8586	34	5	168	Septicemia following leg ulcer. Terminal pneumonia	4 hr. 0 min.	0	1 cm. plus
6. L. K.	K 11090	41	8	157	Chronic diffuse nephritis with uremia	8 hr. 16 min.	4-plus	0
7. F. A.	K 7607	19	0	160	Shock following lobectomy for bronchiectasis	3 hr. 45 min.	0	4 cm. plus
8. M. F.	K 11774	24	0	170	Sudden death 45 minutes after tonsillectomy	4 hr. 30 min.	1-plus	2 cm. plus

*Arranged in order in which subjects were obtained.

TABLE II. DESCENT OF UTERUS FOLLOWING DIVISION OF SUPPORTS

Note the varying sequences in which the various uterine supports were severed. Also that uterine descent occurred when parametrial and paravaginal tissues were divided, and did not occur to any marked degree with division of the structures attached to the fundus of the uterus even when they were the last structures to be cut.

UTERINE SUPPORTS	CADAVER NUMBER	ORDER OF DIVISION OF SUPPORTS								MEASURED DESCENT IN CENTIMETERS (CONSTANT TRACTION OF ONE KILOGRAM ON CERVIX)								
		1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8	AVERAGE
Round ligament		1	6	1	3	2	5	2	5	0.25	0.50	0.00	0.25	0.00	0.50	0.00	0.50	0.3
Ovarian and infundibulopelvic ligament		2	5	2	4	4	6	2	5	0.25	0.00	0.00	0.25	0.70	2.25	0.25	0.25	0.5
Parametrial	Upper one-third	*	5	3	5	4	3	3	6	†	0.00	0.00	0.00	0.00	0.00	0.25	0.25	0.1
	Lower two-thirds	5	3 6	6	6 2	5	3	5	3	1.00	1.25 9.00	2.50	4.50 1.70	4.50	2.00	0.50	2.50	3.6
Paravaginal	Upper one-third	*	2	7	2	5	*	6	*	†	1.25	2.50	1.70	4.50	†	6.00	†	2.6
	Middle one-third	*	*	8	*	*	*	5	*	†	†	2.50	†	†	†	6.00	†	4.3
Uterosacral ligament		3	4	4	*	1	4	4	4	0.00	1.00	0.00	†	0.30	1.50	0.50	4.50	1.1
Pubocervical ligament		4	1	5	1	3	2	1	1	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.1
Vaginal circumcision		6	*	*	*	3	1	*	2	†	†	†	†	†	†	†	†	†

*Support not cut.
†Measurement not obtainable.

pelvic, and the upper portion of the broad ligaments hardly affected the position of the uterus in the pelvis. In three cadavers in which all parametrial and paravaginal tissues were severed, but the round ligaments were left intact, the cervix prolapsed through the introitus without even tensing the round ligaments. Because of the laxness and extensibility of these ligaments it is difficult to see how they can possibly affect the position of the fundus. Hence from an anatomic standpoint the fundus of the uterus is a movable organ. This view is held by Halban and Tandler,[4] who feel that because of this mobility it is impossible to speak of a definite uterine position.

The uterosacral ligaments furnished a small amount of support, which may be explained by the fact that they are so closely connected anatomically to the parametrial tissues. The so-called pubocervical ligaments played a negligible rôle.

The pelvic diaphragm and the pelvic floor remained intact in all eight cadavers and in no instance interfered with uterine descent. Since the integrity of the pelvic floor was not interfered with in any of the experiments and since in every case traction of 1 kg. effected complete uterine descent after all uterine connective structures were divided, it is doubtful whether the pelvic floor affords any support to the uterus. Even in Subject 8, a virgin, the uterus prolapsed completely when the paravaginal and parametrial tissues were cut.

Division of the parametrial and paravaginal tissues, comprising the lower two-thirds of the broad ligament and the upper two-thirds of the paravaginal structures, allowed an average uterine descent of 10.5 cm. *Marked descent of the uterus amounting to actual prolapse never occurred so long as any part of the upper two-thirds of the paravaginal and/or lower two-thirds of the parametrial tissues were intact.* In three instances all of the structures above the vagina were severed, so that the sole support of the uterus was its attachment to the vagina, and in one of these instances only 1 cm. of the circumference of the vaginal wall remained attached to the otherwise completely free uterus. Nevertheless, noticeable descent did not occur. In two of these three cadavers dissection of the paravaginal tissues was carried out from above downward. In each instance, as the vagina was freed it inverted, and progressive prolapse to complete vaginal inversion followed. In two instances in which the vagina was circumcised at its cervical attachment and the parametrial tissues were allowed to remain intact, no descent of the uterus occurred.

The abdominal cavity may be thought of as a bucket, to a hole (vulva) in the floor of which a flexible tube extending upward (vagina) is attached. If the bucket were filled with oysters, or some similar semifluid material, it is obvious that the flexible tube would immediately turn inside out like the finger of a rubber glove, but if this tube were fixed by fibrous bands (paravaginal tissues) to the side walls of the bucket, it would necessarily remain in place. The perineal musculature is merely the bottom of the bucket, and is therefore unable to support anything except the external end of the vagina.

DISCUSSION

Mackenrodt[7] felt that the parametrial and paravaginal tissues were the primary supports of the uterus and noted that ". . . . the pelvic fascia sends out firm bands to the cervix uteri and the vagina, holding and fixing them . . . ."

Fothergill[2] also recognized the importance of the tissues investing the vagina and the lower part of the uterus, though his attention was concentrated on the parametrial tissues. The reasons for his opinion are admirably given, as follows: "To the clinical observer, the nature of these real supports is revealed by the operation

of vaginal hysterectomy. . . . Let him incise the vaginal wall right around the cervix, and, after opening the pouch of Douglas, let him freely divide the posterior attachments. Further let him separate the bladder completely from the uterus and make a wide opening into the uterovesical pouch. The uterus cannot as yet be pulled down much more than before the operation was begun. The something which supports the uterus has not as yet been divided. Next let the operator deliver the fundus through the anterior portion of the incision. This affords another proof that the broad ligaments and round ligaments have no value as suspenders, for they come down freely and without being stretched. Let them be tied and divided, and the uterus still remains fixed by the tissue known as the parametrium, and by this alone. Until this is divided on either side the organ is, for practical purposes, as completely supported as before an incision was made.''

This opinion is correct as far as it goes, but the present experiments show that the paravaginal support is fully as important as the para-

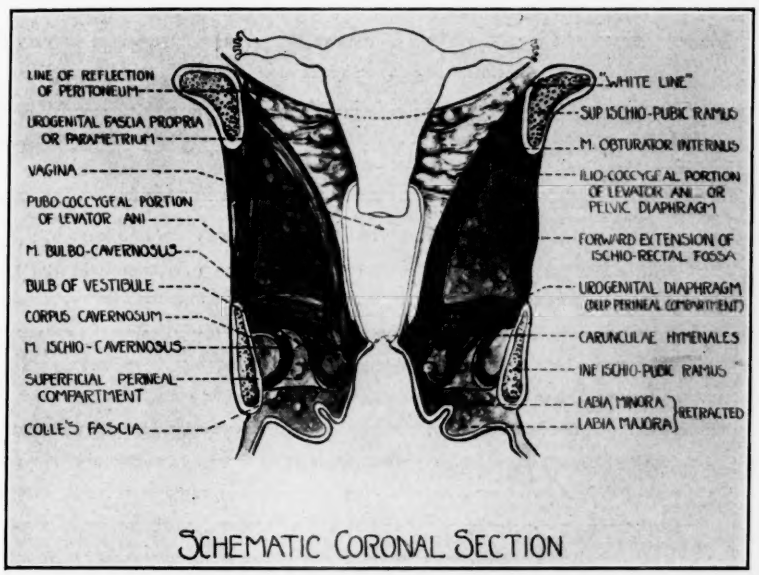

Fig. 1.—Modified by E. W. Scheldrup from an original drawing by H. J. Prentiss. Note the fan-shaped paravaginal and parametrial tissues, or urogenital fascia propria, extending almost from the bottom of the vagina to a point slightly higher than halfway up the uterus. This tissue derives support from the iliococcygeal portion of the levator ani muscle, or the pelvic diaphragm.

metrial, if not more so. Sixty-five per cent of the average descent (10.5 cm.) which occurred when both the parametrial and paravaginal structures were divided was referable to loss of the latter. Furthermore, in three instances in which all of the uterine connective structures above the vagina were severed, noticeable descent did not occur, indicating that the vagina not only has its own support but can maintain the uterus as well. Bonney[1] recognizes the importance of the paravaginal tissues as a supportive medium and describes them as ". . . . two fan-shaped expansions of fibromuscular tissue, which, arising on each side along the whole length of the lateral vaginal walls above the

levator diaphragm as high as the supravaginal cervix, are inserted into the fascia covering the side walls of the pelvis along the lines of attachment of the levatores ani muscle." These parametrial and paravaginal tissues are well shown in a schematic coronal section of the

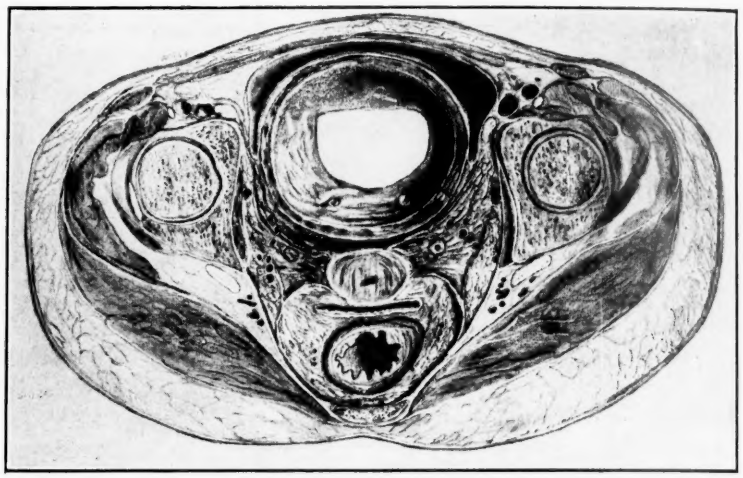

Fig. 2.—Original drawing from cross-section of female cadaver in the Department of Anatomy. Note how the paracervical tissues extend and expand laterally to the pelvic diaphragm. The ureter and pelvic vessels may be seen in this tissue. The exact level of the section may be determind by noting the peritoneum of the bottom of the pouch of Douglas between cervix and rectum.

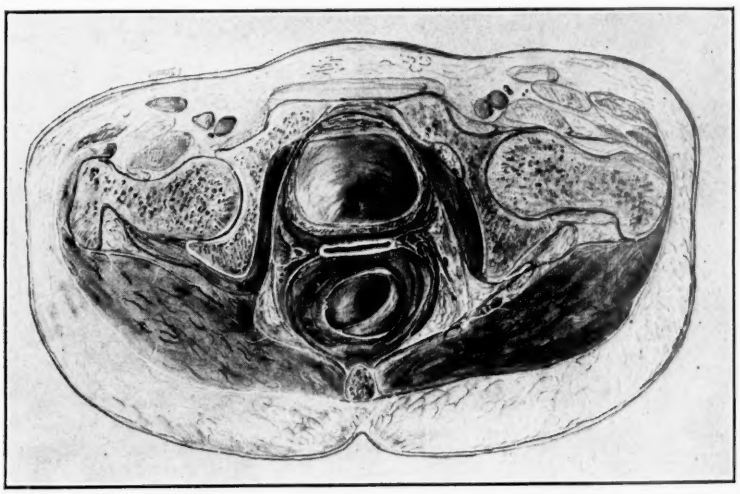

Fig. 3.—Original drawing from cross-section of female cadaver in the Department of Anatomy. Note how the paravaginal tissues are thinner and do not extend laterally as far as they do in Fig. 2 because the pelvic diaphragm is becoming narrower at this point. This will be more readily understood by comparing with Fig. 1, the coronal section.

female pelvis (Fig. 1), and also in cross-section (Figs. 2 and 3). It will be seen that they surround the vagina and fill in all of the space medial to the muscles of the pelvic diaphragm.

The parametrial and paravaginal tissues are identical anatomic structures. The latter are merely continuations of the former, and separate terms are used only for greater exactness in localization. Many names have been given this tissue, such as endopelvic fascia, urogenital fascia propria (Prentiss[8]), cardinal ligaments, etc., but to avoid confusion the descriptive terms "parametrial and paravaginal tissues" are used.

There has been much discussion concerning the nature of these tissues.

Spalding[9] speaks of a definite vesicovaginal fascia, whereas Goff[3] feels that there is no tissue in the walls of the vagina, urethra, bladder, and rectum which can logically be termed fascia. However, he thinks that there is a thin layer of fascia of the areolar type between the anterior vaginal wall and bladder and between the posterior vaginal wall and rectum. Koster[5] in a study of the recto- and vesicovaginal septa finds ". . . . no evidence of existence of any fascial structure comparable to that described in any of the texts." He does find, however, ". . . a loose, areolar connective tissue which can have no restraining or supportive value." Fothergill[2] believed that ". . . . the fascia should be regarded as the sheaths of the muscles, the vessels and the viscera." Bonney[1] says, "The description of them [cardinal ligaments] as perivascular sheaths is altogether wrong, for they not only lie considerably below the uterine arteries as the latter proceed from the hypogastric arteries to the sides of the uterus, but they contain no vessels to speak of."

A continued discussion of the nature of this tissue and whether it is fascial or loose areolar connective tissue is outside the scope of this paper. From the present study of eight female cadavers it appears that when the upper two-thirds of the paravaginal and the lower two-thirds of the parametrial structures are divided, a 1 kg. weight attached to the cervix is sufficient to cause an average uterine descent of 10.5 cm. It is of little moment whether this tissue should be classified histologically as ligament or fascia. The important point is that *it did support the uterus in eight fresh cadavers.*

SUMMARY AND CONCLUSIONS

1. The following experiment was performed on eight female cadavers, none of which had prolapse: After attaching a 1 kg. weight to the cervix, the paired structures attached to the uterus were severed in varying sequences and the resulting uterine descent measured.

2. Section of the round, ovarian, infundibulopelvic, and the upper third of the broad ligaments hardly affected the position of the uterus in the pelvis.

3. The pelvic floor, although it was never incised, did not hinder experimental prolapse of the uterus, and therefore could not have contributed to uterine support in any of the eight subjects.

4. Section of the parametrial (lower two-thirds of the broad ligament) and the upper two-thirds of the paravaginal tissues allowed an average uterine descent of 10.5 cm.

5. Marked descent of the uterus amounting to actual prolapse never occurred so long as any part of the upper two-thirds of the paravaginal and/or lower two-thirds of the parametrial tissues were intact. Of these two arbitrary divisions of the urogenital fascia propria, the paravaginal tissue seemed to be slightly more important, for its division allowed an average uterine descent of 6.9 cm. as compared with 3.6 cm. following division of the parametrial tissues.

Acknowledgments: This study could not have been carried to a conclusion without the generous cooperation of the Department of Pathology and especially of its Head, Dr. H. P. Smith. The drawing of the coronal section of the pelvis was kindly prepared by Dr. E. W. Scheldrup of the Department of Anatomy.

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A SYNDROME SUGGESTIVE OF ESTROGENIC DEFICIENCY*

A Clinical Study

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DETAILED clinical study of a group of patients nineteen to eighty-one years of age who presented themselves with various types of menstrual or reproductive disturbances revealed a large group of subjective symptoms which were very similar in each instance regardless of the menstrual abnormality of which the patients complained. The symptoms were characteristic of those occurring in association with the menopause, and although present in the greatest number and with the greatest severity in the menopausal patients, were also encountered in the younger group of women in association with other menstrual and reproductive disturbances.

The above observations in addition to the uniformly excellent results which have been obtained in the relief of the same symptoms in association with the menopause[1] served as the basis for considering their presence whenever encountered as indicative of estrogenic deficiency and the attempt to correct them by means of estrogenic therapy.

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

The enumeration of the subjective symptoms and several associated conditions and the frequency with which they occurred in the present series of 85 patients follows:

SUBJECTIVE SYMPTOMS	INCIDENCE
1. Exhaustion, tire easily	80
2. Irritability and nervousness	81
3. Emotional instability (weeping, depression, suicidal tendency, disturbing dreams)	69
4. Backache	43
5. Headache (migrainoid)	29
6. Insomnia	16
7. Soreness of breasts	39
8. Leg pains	18
9. Nausea or vomiting	23
10. Cramping	31
11. Vaginal irritation	17
12. Hot flashes	18
13. Decrease or lack of sexual desire	13
14. Decrease or lack of normal sexual reaction	16

ASSOCIATED CONDITIONS	INCIDENCE
1. Acne	5
2. Arthritis	19
3. Colitis	15

The favorable results of estrogenic therapy in the menopause have been demonstrated and accepted, and nothing further will be added at this time. Eighteen menopausal cases were included in the series as a basis for comparison with the remaining 67 younger women from nineteen to forty-three years of age. The symptoms previously enumerated are vividly descriptive of a type of patient with whom we are all familiar, i.e., the tired nervous woman, who, married or unmarried, presents with many of the above symptoms some form of maladjustment of marital or sexual life. Physical and laboratory examination revealing no abnormalities, our only solution has been to assure her of the absence of findings, inform her that she is just "tired" or "nervous" and suggest rather dubiously that rest and a "tonic" may be all that is needed with the result that the derangement either adjusts itself spontaneously or becomes progressively worse.

The syndrome as indicated by the history may be either primary or secondary, in some patients being present since adolescence and in others being initiated or exaggerated by subsequent menstrual or reproductive events. They have therefore been classified according to reproductive types for further consideration.

	NO. OF CASES	AGES
Type I. Nulliparous	19	21 to 36
Type II. Parous	27	19 to 43
Type III. Immediate postpartum	5	25 to 34
Type IV. Sterility	12	23 to 38
Type V. Menopausal	18	30 to 81

Type I. Nulliparous.—The menstrual history in 16 instances indicated the presence of primary estrogenic deficiencies. In the remaining 3, the deficiency was secondary.

The symptoms consisted principally of prodromal exhaustion, nervousness, irritability, emotional instability, cramping, tenderness of the breasts; with leg ache, backache, and headache occuring in the more severe types.

Type II. Parous.—The history of estrogenic deficiency usually dated back to previous pregnancies but frequently indications were obtained that the deficiency had existed since adolescence. The symptoms were usually not of a severe type.

Type III. Postpartum.—These patients presented the typical clinical picture frequently encountered within six or eight weeks following delivery, with extreme emotional instability, exhaustion, nervousness, and usually giving a history of an exceptional feeling of well-being during pregnancy.

Type IV. Sterility.—There were ten primary and two secondary sterilities. Many of these patients had been under treatment over considerable periods of time before glandular therapy was started. Tubal occlusions, aspermia, and the other usual causes of sterility had been eliminated. The symptoms exhibited were mostly prodromal and in almost every instance dated back to adolescence. Uterine hypoplasia was frequently an accompanying condition. In only two of these patients were the symptoms of the severe type.

Type V. Menopausal.—Nine of these menopausal cases were spontaneous, 4 were due to irradiation and x-ray therapy, and 5 resulted from surgical removal of the ovaries. The symptoms were in most instances of the severe type. This was particularly true of the surgical and x-ray radium group and of those cases in which symptoms of estrogenic deficiency had been present for long periods of time prior to cessation of the menses.[2]

Further classification according to the severity of symptoms:

Group I. *Mild.* Mild prodromal symptoms only, 28 cases.
Group II. *Moderately severe.* Prodromal symptoms. Some symptoms present throughout cycle, 36 cases.
Group III. *Severe.* Severe prodromal and constant symptoms, 17 cases.
Group IV. *Exaggerated.* Extreme and constant symptoms, 4 cases.

ESTROGENIC SUBSTANCES USED

The materials used in this study consisted of an oral and a parenteral preparation of estrogenic substance. The oral preparation "Emmenin" (Collip*) is obtained from the human placenta and according to Collip[3] "comes nearer to being a physiologically active substance than the crystalline compounds ketohydroxy (theelin) and trihydroxy (theelol) estrin." Collip has suggested the possibility that emmenin is produced in the human placenta as the parent estrogenic substance and that the crystalline products "theelin" and "theelol" may be regarded as the end-products of metabolism. Bauer, Kantor and Klawans[4] have demonstrated that the response in bringing down the ovipositor of the Japanese bitterling of emmenin (Collip) and progynon (Schering) was greater per unit used than the reaction produced by the more refined crystalline products di-tri and ketohydroxy estrins. For parenteral administration, amniotin in oil, 8,000 I.U. per 1 c.c. (Squibb*), was used

*The large amounts of emmenin supplied by Ayerst, McKenna & Harrison, Ltd., and preliminary amounts of amniotin supplied by E. R. Squibb & Sons have made this study possible and are greatly appreciated.

as an adjunct to the basic oral therapy. Complete data regarding the commercial preparations available are presented in the *Journal of the American Medical Association,* August 31.[5]

TREATMENT

Therapeutic results in this series were greatly enhanced by the fact that it was composed entirely of private patients from whom it was possible to obtain intelligent cooperation. They were informed that even though they obtained prompt relief of symptoms, it would be necessary to continue some form of therapy for at least four to six months to obtain permanent results.

The varying degrees of deficiency encountered necessitated the development of a generalized therapeutic plan which could be varied in accordance with the degree of deficiency present as indicated by the symptomatic response. The basic treatment consisted of the oral administration of "emmenin" (Collip). The patient was instructed to take one dram 20 (day-oral) units three times daily in one-half glass of water one hour before meals except during the time of the menstrual flow, emphasis being placed on the necessity for resuming the oral medication immediately after cessation of each menses.

It was determined that the most favorable time to begin the therapy in all except the amenorrheic patients was during the phase of follicular activity or immediately following the cessation of the menstrual period. In many instances, particularly when the subjective symptoms were mild in character, partial or complete relief was obtained within forty-eight hours. Failure to obtain complete relief, or recurrence of the symptoms at any time prior to the next menstrual flow, was used as an indication for the addition of parenteral therapy. Amniotin in oil, 8,000 I.U. was administered as frequently as necessary to produce complete relief of symptoms. The amount of parenteral therapy ranged from 8,000 to 32,000 I.U. daily, and was increased or decreased as indicated by the response of the symptoms. It was found that the greatest amounts were necessary at the times when normal estrogenic depletion occurs, either at the time of ovulation or immediately preceding the menstrual periods. After relief of the subjective symptoms had been obtained, the need for parenteral therapy decreased rapidly. Subsequently occasional injections were necessary only at the time of greatest estrogenic depletion and it eventually was found possible to maintain freedom from symptoms by oral therapy only, even in the Group III cases.

Although sufficient time has not elapsed with most of the cases in this series, permanent results are being obtained by means of a small maintenance dose, with the possibility that medication may eventually be stopped entirely. This is indicated by the results of Severinghaus and

others in the treatment of involutional states and by the realization that conditions encountered in this series differ from the actual menopausal conditions only in degree of estrogenic deficiency.

RESULTS

Twenty-eight cases classified as *mild* in Group I were relieved of symptoms by oral therapy only, and it was found possible to maintain freedom from symptoms with gradually decreasing amounts.

In the 36 *moderately severe* cases in Group II, the same results were obtained by addition of parenteral administration varying from 1 to 10 injections of amniotin in oil. In this series also it has been possible to maintain freedom from symptoms by means of the oral preparation emmenin after the initial relief has been obtained.

In Group III, in 17 cases classified as *severe,* similar results were obtained, the only difference being that results were not obtained as promptly, larger amounts of parenteral therapy were necessary, and remissions occurred more frequently before oral therapy became adequate. The parenteral therapy in some instances amounted to 32,000 I.U. daily.

In Group IV, in the 4 cases of the *exaggerated* type, incomplete results were obtained and these four cases were listed as the only failures in the series. In two cases the treatment was discontinued before sufficient therapy had been administered, which may have been the cause of failure. One of the remaining two cases was found to have an adrenal deficiency and is at present being treated by combined estrogenic and adrenal therapy. The other failure was found to have an accompanying thyroid deficiency as manifested by a basal metabolism rate of –19 and cholesterol of 200, although subsequent therapy has not been started.

It is of interest that as associated conditions, acne occurred in 5 patients, arthritis in 19, and colitis in 15, and in every instance where the subjective symptoms were relieved and the treatment continued, all of these associated symptoms disappeared usually within a few days or weeks. In the group of sterility patients, 4 of 12 have become pregnant after from three to six months of therapy. These patients have not as yet completed the pregnancy and will be reported at a later date.

In no instance has it been necessary to resort to additional treatment for dysmenorrhea, menorrhagia, metrorrhagia, or the secondary amenorrheas. Whenever encountered they were either corrected or improved to the extent that they were rendered negligible. Although not encountered in this series, other pelvic pathology must be considered in the presence of the above symptoms before estrogenic therapy is instituted.

Massive doses of amniotin have been administered in amounts up to 72,000 I.U. daily in the patients with the extreme symptoms of estrogenic deficiency without the production of bleeding or other visible ill effects. This would undoubtedly not be true if attempted in patients

where no deficiency existed. The only evidence of overdosage that has been observed has been a delay in the menses of from two to eight days, and reduction of dosage in 5 cases where this occurred was followed by return to normal.

COMMENTS

The results obtained can be explained only on a theoretic basis if we accept and consider certain experimental evidence.

It is known that the ovary produces at least two hormones, a follicular or estrogenic hormone "estrin" and the corpus luteum hormone "progestin" or "corporin." It has been demonstrated that one of the actions of estrin is inhibition of the activity of the anterior pituitary gland and that progestin either neutralizes or causes the excessive elimination of estrin.[7] It is known that the anterior pituitary maintains a controlling action over the other glands of internal secretion and that it produces follicle stimulating and luteinizing hormones which act directly on the ovary.

The multiplicity of symptoms encountered can be explained only when we consider that the estrogenic deficiency causes the removal of the normal inhibition to the anterior pituitary gland and thereby permits derangement of function of the entire glandular system, and as maintained by Severinghaus,[6] correction of this deficiency by estrogenic therapy replaces the normal inhibition of the anterior pituitary gland which in turn causes a return to normal of the entire glandular system with relief of symptoms. Where failures have been encountered or only partial success obtained, the indicated explanation would be either insufficient estrogenic therapy with inability to entirely control pituitary activity, or depletion of some other gland such as the adrenal, thyroid, or parathyroid to the extent that these glands no longer respond to normal pituitary control.

It is again desirable to call attention to the fact that the data presented are the results of clinical observation not substantiated by quantitative determination of estrin and prolan content of the blood and urine, or by examination of endometrial tissue. Methods available for these determinations have contributed greatly to our knowledge of glandular function but due to their complexity and highly technical nature are not available for routine application.

Although conclusions based only on clinical results are frequently misleading, it is felt that the inferences indicated by the results of the present study are to a certain extent justified by the accumulation of laboratory and clinical evidence of the past five years. Preparations are being made to carry on the present work under the added control of blood and urine determinations of estrin and prolan in an attempt to prove or disprove the following conclusions and to obtain additional information.

CONCLUSIONS

1. A syndrome composed of subjective symptoms is presented which occurs not only in association with the menopause but also accompanying menstrual and reproductive disturbances in young women.

2. The correction of these symptoms in a large proportion of 85 patients by the oral and parenteral administration of estrogenic substances indicates that this syndrome is strongly suggestive of estrogenic deficiency.

3. In many of the patients in this series, dysmenorrhea, secondary amenorrhea, menorrhagia, metrorrhagia, and sterility have responded to estrogenic therapy.

4. When relief of subjective symptoms was used as a criterion for the amount of estrogenic therapy necessary, no evidence of permanent harmful effects of massive dosage was observed.

5. The excellent results obtained by the administration of an active oral estrogenic substance and the added difficulties and economic factors involved when parenteral therapy is necessary, emphasize the need for an oral estrogenic preparation of greatly increased concentration and potency, not to replace the preparations now available, but to be used as an adjunct wherever necessary.

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DISCUSSION

DR. LAWRENCE RANDALL, ROCHESTER, MINN.—There are two groups of patients with evidence of disturbance in the physiology of the genital tract, those who have associated symptoms and those who do not. The majority of the former have laboratory evidence of pituitary hyperfunction with or without definite proof of lack of estrin. The second group does not show evidence of excess pituitary function, but usually has evidence of pituitary failure and an absence of estrin.

The chief example of the first group is the woman in the menopause. The familiar symptoms are present, estrin may still be detected in the blood and urine, but the Aschheim-Zondek prolan test is positive. The best example of the second group is the amenorrheic but otherwise healthy and symptomless young woman. She will usually be found to have no evidence of either prolan or estrin in the blood or urine and to have an atrophic uterus. I would therefore regard the syndrome described by Dr. Schneider as one suggesting pituitary hyperfunction, rather than one suggesting estrogenic deficiency.

We have seen instances of women with fifteen rat units of estrin per liter of urine, who had a positive Aschheim-Zondek prolan and who had symptoms in general similar to those that Dr. Schneider mentions. On the other hand, in a primary pituitary failure with no evidence of prolan or estrin, these symptoms are rarely, if ever, seen.

We have some eighty patients whose symptoms correspond closely with Dr. Schneider's group, but all of these patients have shown a fairly normal estrin content of the urine. Biopsy of the endometrium in many instances has borne this out. In this group, however, thirteen of twenty-one had evidence of excess pituitary function.

DR. JEAN PAUL PRATT, DETROIT, MICH.—About ten years ago I reported what I thought might be success with small doses of estrogenic hormone. In my first experiments I was misled into believing that very fine results were obtained, but with a careful check, I found the results were quite disappointing.

It seems increasingly difficult to know what symptoms to attribute to the menopause. A group in Chicago reporting on 1,000 women found that 85 per cent had no interruption of daily routine at the time of the menopause and only 15 per cent showed symptoms. If all these symptoms mentioned are due to interruption of ovarian function, it seems strange that the symptoms are so widely different in various individuals and so frequently entirely absent.

In our own hospital when some physician has made a diagnosis of menopausal symptoms, I ask him to observe the patient carefully and then send her to me for therapy. I will not tell him what therapy is to be employed. I have a preparation of theelin in oil and the same kind of oil without theelin sterilized and ready for injection. Just as much improvement has been noted with the oil without the theelin as there is with the theelin in the oil. I am not the observer, for the physician who refers the patient is the one who makes the notes on the change of symptoms. That is something that needs to be explained.

It has been known empirically for years that thyroid therapy has improved many of these patients. Quite recently it has been found that the ovary contains a far higher percentage of thyrotropic substance than the thyroid. So we now have another field open for investigation, namely, the thyrotropic hormone in the ovary.

There is also no question but that these women are psychically disturbed, and it seems to me that this comes back to something fundamental in the person. It seems important to correct psychic causes together with the others mentioned.

I believe there is a wider basis for menopausal symptoms than the lack of estrogenic substance in the ovary.

DR. MARK T. GOLDSTINE, CHICAGO, ILL.—Six years ago I started making a placental extract by practically the same method as that of Collip. In attempting to break down our placental extract for crystallization we also obtained a cloudy product which is comparable to Collip's APL but which we found had very little potency. Some of the men who were using this placental extract were given the new APL product and in a short time they corroborated our findings that APL had very little potency.

Does emmenin contain only follicular substance or does it also contain a great deal of the gonad-stimulating part of the placental extract? If the latter is true, we should be rather careful in administering it to young patients. I know from experience that some young women's ovaries are sensitive to placental extract and with large enough doses we can produce necrosis of the ovary. I am therefore going to be very cautious in the length of time I give emmenin in the dysmenorrhea cases. We have never used our own placental hormone except for functional bleeding. We have never used it for sterility.

DR. CARL P. BAUER, CHICAGO, ILL.—In our work it has been rather interesting in testing these various preparations on the reaction of the ovipositor of the bitterling to find the purer the product is the larger doses we have to use in order to produce a positive reaction. There is no question in my mind that there is something in the urine of pregnant women and also in the urine of women at various

times in the menstrual cycle that is not entirely like some of the estrogenic products. It takes only 45 units of emmenin, while it takes 450 rat units of follicular hormone, to produce a reaction in the bitterling.

If the gonadotropic principle in urine is destroyed by boiling, an estrogenic principle remains which represents all the elements present in the human pregnancy urine. If one purifies the hormone it eliminates the substance which may possibly relieve the symptoms. This is the reason we get failures with some preparations and good results with others.

DR. SCHNEIDER (closing).—The fact that our results in the treatment of the involutional states have been greatly improved with the use of more potent materials and greater dosages is I think an indication that the treatment is not entirely psychic. I should like to emphasize that more consistent results may be obtained in dysmenorrhea, amenorrhea, menorrhagia, and metrorrhagia, by the treatment of the subjective symptoms with estrogenic substances than according to our experience is possible with anterior pituitary and anterior pituitary-like substances.

The question which has been raised as to the possibility of placental extracts containing some of the gonadotropic factors probably does not apply to the preparation "emmenin" due to the fact that the gonadotropic factors can be removed by boiling.

Further evidence that estrogenic deficiency is a basis for these symptoms is that many of our patients give a history of a feeling of well-being during pregnancy when large amounts of estrin are produced by the placenta.

THE EFFECTS OF X-RAY AND RADIUM ON CANCER OF THE CERVIX*

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IN 1930 a new routine in the radiation treatment of cancer of the cervix was adopted on the Gynecological Service of the Barnard Free Skin and Cancer Hospital in charge of Drs. G. Gellhorn and F. J. Taussig. Prior to this, external irradiation with roentgen rays was used only occasionally after radium therapy. Radium was used in dosages of 4,500 mg. hours or less, the filtration consisting of a maximum of 1 mm. brass, and a minimum of bare steel needles. When this study was started, external irradiation with roentgen rays was given each patient, the radium applied three weeks following the roentgen therapy in one massive dose of from 4,500-6,000 mg. hours, and the filtration changed to heavy gold having a density equivalent to 1.2 mm. platinum. As a rule 150 mg. of radium were used divided between cervical canal and uterine cavity, but not evenly. At times smaller amounts of radium used over longer periods of time were used to give the desired dosage. Toward the end of this study the 150 mg. of radium were divided into four portions, one part being placed in the uterine cavity, one part into the cervical

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canal, and the other two parts being placed in each vaginal fornix. The vaginal portion of this radium application was filtered by 2 mm. of platinum equivalent. It is my opinion that the latter method is the one giving the best clinical results but not enough patients were treated in this manner to justify more than a personal opinion.

Every new patient entering the clinic with a diagnosis of cancer of the cervix had a biopsy regardless of the extent of the lesion. Of 114 cases studied, 102 patients were inoperable. About 25 per cent were placed in clinical Group IV (Schmitz classification). During the two and one-half years that this study was in progress, about 250 new patients with cancer of the cervix were seen and treated but only those are now being considered who were treated by x-ray and radium, and in whom it was possible to continue the investigation by microscopic study after the radium therapy. About 135 patients treated are not included in this report, because they either had a radical operation, or they did not report back to the clinic at the proper time after they had been treated with radium.

PROCEDURE

After examination and biopsy each new patient was sent to the x-ray department for a course of treatment. Each patient received a dose of between 700 r. and 1,500 r. Larger doses were not given because the great number of patients being treated in this institution taxed the machine to capacity. There were no marked skin disturbances in any case. The patients withstood the effects of the deep therapy very well. Occasionally it was difficult to convince the patients that radium therapy was necessary, for their symptoms had disappeared after the x-ray treatment. Clinically the result of deep therapy was a marked diminution in the size of the lesion, and a marked decrease in the secondary infection usually present in advanced cancer of the cervix. About three weeks after the deep therapy was completed the radium was applied. Another biopsy was taken at this time. It was noted at the time of the radium application that there was much less bleeding on manipulation than in patients who did not receive deep therapy. After being discharged from the hospital, the patients were instructed to return for observation at two- to three-week intervals. When six weeks had elapsed another biopsy was made. This last biopsy was of considerable value in deciding the future treatment of the patient. Those patients in whom cancer could be demonstrated microscopically were immediately reradiated by either emanations, radium, or additional deep therapy. It was not uncommon to find cancer microscopically in the cervix of patients who were apparently locally free of the disease by the ordinary methods of examination. By reason of early reradiation we feel that certain patients are now living and clinically free of cancer that would have gone undiscovered and untreated for some time had not these routine biopsies been made. Other patients had local healing in spite of their far-advanced condition. In the beginning of this study it was felt that x-ray and radium should cause local healing in every case, but we have found that certain types of cancer are so radio-resistant that it is impossible to cause a disappearance of the cancer microscopically regardless of the amount of radiation used. We were unable to determine in advance which grade or type of cancer microscopically would not respond to radiation therapy.

By taking biopsies for microscopic studies at definite intervals during the treatment, we noted a difference in the healing process with the use of different filters

surrounding the radium. When 1 mm. of brass was used with a total radium dosage of from 4,000-4,500 mg. hours, clinically a large, sloughing, necrotic area remained in the cervix and vagina for many months despite the absence of demonstrable cancer. Epithelial regeneration was extremely slow so that a discharge annoyed the patient for long periods of time. The cause for this was discovered soon after these routine sections were studied and compared with similar sections taken after radium of the same or larger doses filtered through 1 to 2 mm. platinum equivalent instead of 1 mm. brass. Clinically with the heavier filtration there was rapid retrogression of the local lesion with complete healing in from four to eight weeks. The crater, when present originally, had disappeared, leaving a more or less normal-appearing cervix. Usually with these heavy filters redness was the only sign of radium having been used. In the tissue radiated through brass, a dense fibrosis with an endarteritis completely occluding the vessels is seen microscopically, so that the blood supply to the surface is insufficient to maintain an epithelial regeneration whereas in the tissue radiated through the gold or platinum a soft fibrosis takes place. In this tissue, although an endarteritis is also present, it is to a much lesser degree so that the vascularity of the tissue is not greatly impaired and the epithelial regeneration can be seen in practically all of the sections. These histologic pictures explain the difference observed clinically.

When a filter of lesser density such as 1 mm. brass is used, a fairly large amount of beta radiation is not absorbed and is accordingly transmitted into the tissues. These beta rays are similar in action to the hot cautery and cause destruction of normal and cancer cells alike, thereby increasing the likelihood of fistula formation. By the use of filters of 1.5 mm. 18 karat gold, practically 100 per cent of the beta rays are absorbed and the tissues receive 100 per cent gamma radiation. The clinical application of this principle is proved by the marked reduction in the number of vesicovaginal and rectovaginal fistulas due directly to radium since the use of heavy filters. Prior to 1933 the production of fistulas by radium was not uncommon. Since this time only one fistula has been produced directly by radium. This patient had a moderately advanced type of tumor which showed some slight microscopic changes from the preliminary course of x-ray. The tumor was Graded II (Broder's classification), which is not supposed to be radiosensitive. She received 5,000 mg. hours of radium filtered with 1.5 mm. 18 karat gold and 1 mm. rubber, but in spite of the heavy filtration, the relatively small radium dose, and the radioresistant type of tumor, a fistula rapidly opened and has remained so until the present time. The patient has gained more than thirty-five pounds in weight and has been clinically free of cancer for more than two years. We feel that this fistula developed because of overradiation, although prior to treatment there were no indications that the 5,000 mg. hour dose of radium would not leave a sufficient margin of safety.

In a previous publication dealing with histologic grading in carcinoma of the cervix we concluded that grading alone was of no prognostic value, although in other portions of the body, such as the lower lip, there was a definite relationship between grade of tumor and prognosis. Additional material for a continuation of this study became available with these cases. New cases were classified, according to the clinical extent of the disease, into four groups, and also into four groups according to their microscopic grade. One hundred fourteen cases were studied; there were 3 adenocarcinoma Grade II, 49 squamous cell carcinoma Grade II, 56 squamous cell carcinoma Grade III, and 6 squamous cell carcinoma Grade IV. Because of the absence of any Grade I cancer in this series

and the relatively few Grade IV cancers, a comparison will be made between the cancers of the other two groups, namely Grades II and III.

From Table I it is seen that 105 of the 114 cases fall into histologic Grades II and III, the cases being almost evenly divided between these two grades. It is of interest to note that the percentage of primary local cure is approximately the same in cancers of these two grades in the same clinical group. This at least suggests that the clinical extent of the tumor is of more importance in estimating the probable local cure than is the histologic grade. The response to radiation in the two his-

TABLE I

HISTOLOGIC GRADE	CLINICAL GROUP	CASES	PRIMARY LOCAL CURE	NO LOCAL CURE	LOCAL CURE BY RERADIATION
Adeno-carcinoma Grade II	Group I	0	0		
	Group II	0	0		
	Group III	2	2		
	Group IV	1	1		
Squamous cell carcinoma Grade II	Group I	1	0	1	1
	Group II	2	2		
	Group III	37	22	15	5
	Group IV	9	4	5	1
Squamous cell carcinoma Grade III	Group I	1	1		
	Group II	6	6		
	Group III	34	20	14	9
	Group IV	15	6	9	1
Squamous cell carcinoma Grade IV	Group I	1	0	1	1
	Group II	1	1		
	Group III	4	2	2	1
	Group IV	0	0		

tologic grades being considered appears to be the same, thereby apparently disproving, at least in these cases, any marked difference in radiosensitivity in cancers of the same clinical extent with different microscopic characteristics. Clinically there are a larger percentage of far-advanced cases in the Grade III class than in the Grade II. This is possibly due to the fact that the more undifferentiated tumor grows faster than the more differentiated one. Of these 114 cases, 67 or 59 per cent showed primary local healing with no cancer demonstrable microscopically after a course of deep therapy and a full course of radium. Of the remaining 47 patients in whom cancer was present microscopically after treatment, 33 were reradiated almost at once. Of these reradiated cases, 19 patients showed local healing. The remaining 14 cases that did not undergo primary local healing were not reradiated either because the patient refused further treatment or her condition did not warrant additional radiation.

Another very interesting result of this study is the result of various amounts of radium on the local cancer. The cases treated with a primary dose of 4,500 mg. hours or less of radium were arbitrarily divided

from those treated with more than this amount of radiation. Seventy-three patients were treated with more than 4,500 mg. hours' radiation with 43 or 57 per cent local primary cures. Forty-one were treated with less than 4,500 mg. hours' radium radiation with 24 or 58 per cent local primary cures. The primary results were practically the same. However, these figures do not reveal the whole truth as the cases were followed periodically, and it was found that whereas 14 per cent of the patients treated with more than 4,500 mg. hours' radiation had any recurrence of cancer in the cervix or vagina, 46 per cent of those treated with less than this amount of radium had local recurrences. Although comparatively small doses of radium may cause complete clinical and histologic regression of cancer in the cervix and vagina, there will be a local recurrence in almost half of the patients so treated. On the other hand, when larger doses of radium are used, there may be no greater number of primary local cures, but there will be comparatively few recurrences in the cervix. It must be clearly understood that a primary local cure after radiation does not necessarily mean that the patient is clinically free of cancer for about one-third of the patients who had completely healed cervices have died of pelvic or distant metastasis without a local recurrence.

It has been stated that there were marked clinical benefits to the patient from the relatively small amounts of preliminary external irradiation with roentgen rays. However, it was not possible to note these changes microscopically to the same degree as they were noted macroscopically. In only about 20 per cent of all patients treated with roentgen rays were there rather marked histologic changes. These changes consisted of the cells becoming degenerated, marked vacuolization, and fibrosis. In an additional 30 per cent of the patients treated there were lesser changes demonstrable, consisting mainly of an increase in the size of the cells with a tendency to become more acidophilic. In the remaining 50 per cent of the patients treated with the same dosage of x-ray, a diminution of the inflammatory process was the only histologic change noted. Had larger amounts of roentgen rays been used we feel quite sure that marked histologic changes would have been seen in all the cases. Such changes have already been described by Healy and Arneson.

The effectiveness of radiation by the gamma rays of radium decreases rapidly as the distance from the source of energy increases. Therefore, knowing the changes that take place in the tissues as a result of roentgen ray therapy, it seems quite logical to assume that it is the best method available for treating the parametrial extensions that exist in most of the patients seen. These tissues can be treated both before and after radium therapy with large amounts of roentgen rays divided into small daily doses given over a long period of time without the danger to the bowel that large amounts of deep therapy given over shorter periods might cause.

SUMMARY

1. One hundred fourteen patients with cancer of the cervix treated with a small course of roentgen ray therapy and varying amounts of radium radiation were studied clinically and histologically over a period of two and one-half years.

2. Eighty-six of the 114 patients treated showed local healing. In spite of extremely large doses of radium, it was impossible to cause local disappearance of cancer in fourteen cases.

3. Almost 50 per cent of patients treated with less than 4,500 mg. hours of radium radiation had local recurrences, whereas there were only 14 per cent recurrences in those patients treated with more than this amount.

4. Additional radiation after failure of the primary radiation to cause local healing is of great value as nineteen of thirty three patients treated in this manner had local cures following reradiation.

5. The roentgen ray therapy given prior to the radium application causes a marked retrogression of the tumor, decreases the amount of secondary infection present, and makes the operation of applying the radium easier.

6. Radium should be filtered with at least 1 mm. of platinum or 24 karat gold when used intracervically, and 2 mm. platinum when used as a surface application in the vagina. This prevents a complete endarteritis and hard fibrosis which in turn prevent healing. It also lessens the danger of fistula formation.

7. There appear to be no marked differences in the response to radium of the cancers of the various histologic grades studied so that histologic grading appears to be of little value in the radiation treatment of cancer of the cervix, although the grade of tumor may influence one in favor of surgery in very early cases. There appears to be no logic in the latter. The clinical extent of the disease is of far greater importance in determining the method of treatment and for prognosis.

8. Roentgen ray treatments in large amounts given over a long period of time should be effective in the parametrial extensions of the disease.

9. Larger doses of radium with heavier filtration apparently cause a greater permanency of the local cure.

637 REPUBLIC BUILDING

DISCUSSION

DR. LLOYD O. HOFFMAN, OMAHA, NEB.—The vital importance of heavier filtration has not been recognized in this country until the last few years. Many of our American gynecologists are still content with 1 mm. brass filter, which allows more beta than gamma rays to reach the surface tissues, giving excessive exudation and sloughing with subsequent endarteritis and fibrosis. At the University of Nebraska four years ago, 0.5 mm. of platinum was being used. Two years ago screenage was increased to 1.0 mm. platinum equivalent by the use of 2.0 mm. of

lead. This screenage is used both for surface and intracavitory application. I should like to ask Dr. Auer if we could expect an improvement in clinical results by an even heavier screenage, such as 2.0 mm. of platinum would give.

Rather routine treatment at the University Hospital consists of an application divided between the cervix and vaginal vault. The vault treatment is with the Curie Colpostat or London Bakelite applicator. No larger quantities than 40 to 60 mg. of radium are used.

As an initial dosage 6,000 to 8,000 mg. hours are used. Patients with good prognosis are irradiated in six to eight weeks with 60 to 70 per cent the original dosage if there is any residual tumor mass on gross examination. A small number of patients have been operated upon after x-ray and radium radiation, a total hysterectomy being performed.

Biopsies have not been a routine procedure, but from the findings disclosed in Dr. Auer's paper, we shall adopt this as a routine measure.

DR. JEAN PAUL PRATT, DETROIT, MICH.—I would like to say a word about the use of hysterectomy in conjunction with x-ray and radium. Our five-year cures of all cases including inoperable ones are about 40 per cent, which is a little higher than the general average. If we analyze our cases, however, we find a little higher percentage of operable cancer than reported by Healy, who has an average five-year cure rate of 22 per cent.

One objection to Dr. Auer's method is that the biopsy is taken close to the place where radium is applied. The site in which the cancer persists is distant from this point and cannot be reached for biopsy.

In two patients treated at another clinic with radiation and hysterectomy by us, the cervix showed definite mitotic figures still present. Two of our own patients treated with radium also showed mitotic figures in the specimen removed at hysterectomy. Therefore, we feel that hysterectomy in conjunction with radiotherapy adds to the margin of safety.

Radiotherapy preceding hysterectomy renders the operation much simpler. The risk of the extensive Wertheim operation is too great to justify its routine use and we employ the simple complete hysterectomy.

DR. RALPH A. REIS, CHICAGO, ILL.—Dr. Max Cutler, who is in charge of our Tumor Clinic in the Michael Reese Hospital, has led us to believe that we will get better results if we use smaller doses in the vagina, in the cervical and uterine canals over a long period. Our treatment consists of 8,000 to 9,000 mg. hours given over a period of eight days followed by external irradiation by means of the four gram bomb. I wish I could paint you a glowing picture. We have had the Tumor Clinic four years and I am not certain that our results are much better than when we were using smaller doses of radium followed by 200,000 volt x-ray therapy.

I do not see how a simple hysterectomy, such as Dr. Pratt suggests, will add anything to our results, because if carcinoma is left in the cervix, it is also left in the parametrial tissue and glands.

I am patiently waiting as we all are for another five years to see whether this tremendous amount of radium is worth all the bally-hoo with which we received it and began to use it.

DR. HAROLD O. JONES, CHICAGO, ILL.—The microscopic picture of tissue removed at biopsy six weeks after radiation seems to me difficult to evaluate. One might have evidence of malignancy after six weeks which would not be present after twelve weeks.

We have not been able to approach Dr. Pratt's 40 per cent of five-year cures by any method, and are still around 23 per cent. Originally we gave five, 6,000 and 7,000 mg. hours, but now we are giving under 4,000 combined with deep therapy. Our results are just about the same.

DR. AUER (closing).—There seems to be no logical reason to expect better results by using a heavier filter, for it has been shown that 2 mm. of platinum will absorb all of the beta rays and a small amount of the gamma rays. Increasing the density of the filter beyond this point only decreases the amount of available radiation.

Last year Dr. Taussig described the removal of the iliac lymph nodes following full doses of x-ray and radium. We believe that this procedure is not a radical procedure because in about 46 per cent of all patients so treated cancer was demonstrated in the glands removed at operation.

Radical operation for the cure of carcinoma of the cervix has a definite place in our armamentarium. Our operative results in early cancer are better than the results following radiation. There has been too great a swing to the side of radiation in most clinics. In our work we have found that about 20 per cent of all patients treated with radium will not respond to this form of treatment. Included in this 20 per cent are cases of Grade IV carcinoma, which are supposedly extremely radiosensitive.

The reason that we took the biopsies at six weeks was that in no patients in whom carcinoma was demonstrated at that time was there a spontaneous disappearance of the cancer in the cervix at a later date.

TECHNIC OF SUCCESSFUL REMOVAL OF THE SEPTUM OF UTERUS SEPTUS AND SUBSEQUENT DELIVERIES AT TERM*

RALPH LUIKART, M.D., OMAHA, NEB.

UTERINE abnormalities in general are thought of and treated as curiosities. Before conception the pathologic significance in most instances is slight. Dysmenorrhea and occasionally difficulty in coitus may be the only symptoms. The purpose of this communication is to describe a technic which is both simple and safe, whereby one type of abnormality of the uterus, in which there is a tendency toward habitual miscarriage and to hemorrhage in pregnancy and labor, can be made to carry a pregnancy to viability. I also wish to report two patients so treated with favorable results.

Every imaginable variation of the uterus may be found; varieties may range all the way from a slight increase in duplication to two distinct uteri with separate appendages and two vaginas, or complete absence. Most of these conditions have been discovered on the operating table, or at autopsy. Anomalies of the fetus are not uncommon products of conception of the abnormal uterus.

Bainbridge[1] states that double uterus is found in about 14 per cent of congenital uterine deformities. The double uterus seems to favor conception. Bainbridge reports Debierre's[2] observation of a woman who bore one child on July 17, 1870, and another October 31 of the same year, both at full term.

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Numerous other cases of infants delivered at term from double uteri are reported in the literature. This is not the case with uterus septus. A thorough search of the literature has revealed practically no successful plastic surgery on the septate uterus, resulting in a uterine body that is adequate to perform its normal function, i.e., first, normal menstruation, and second, permit the uterus to act as an incubator for an ovum, and to successfully give forth a live baby at term.

Von Salaz[3] states that operative unification of the two halves of a uterus duplex by the abdominal route may be considered and authors report normal births following it. However, there is great danger, he states, of the surgical scar in the uterus tearing during pregnancy or delivery, or of disturbance in the uterine contractions, because the two halves of the uterus may contract independently. Warlow and Smith[4] report two cases of uterus duplex bicornis. In both cases, because of dysmenorrhea and complications from pregnancy it became necessary to do hysterectomies. Many similar cases handled in like manner are reported in the medical literature. Steel,[5] in a patient eighteen years of age, found a septum extending from the fundus, dividing the uterus, cervix and vagina, similar to the two cases reported below. He removed the septum in part but reported no pregnancy to term later. Hirst[6] reports a case of uterus subseptus in which he operated after the patient had had three deliveries at six months and one earlier miscarriage. Hirst proceeded by the vaginal route and states that this is the best operation if practicable, because it causes no impairment of the expansive power of the uterine body.

Histologically the fusion of the müllerian ducts should form a symmetrical uterine body with sufficient tissue so that when conception takes place the normal uterine cavity with a capacity of 4 c.c., can increase more than five hundred times, and yet not thin out or overstretch the uterine wall to the extent that there is danger of rupture before term. If there is insufficient uterine tissue involved in the pregnancy either abortion or a miscarriage takes place, or the uterus ruptures when its capacity has reached its limit. This is exactly what happens in tubal pregnancy. In case of a septate uterus, if a pregnancy takes place in one half, the uterine wall of the other half hypertrophies, and by its bulk it may obstruct the delivery from the impregnated half, making serious mechanical difficulty and danger from hemorrhage; or it may be the cause of an erroneous diagnosis, by giving the impression to the obstetrician of a myoma, an ovarian cyst, or an extrauterine fetal sac. If the septum extends only part way down to the cervix from the fundus (uterus subseptus) the ovum may be able to make use of sufficient amount of the uterine tissue to reach term and be born alive. A viable baby is the exception rather than the rule, even in uterus subseptus (DeLee[7]). In such cases unfavorable presentations occur and the fetus often is deformed.

Since lipiodol x-ray of the uterus with pneumoperitoneum has come into use it is much more simple to diagnose and differentiate most uterine abnormalities. Once the proper diagnosis has been made it is

not difficult to determine what surgical procedure, if any, may be helpful, and because of this much better results should be obtained. The accompanying lipiodol x-ray and diagram help visualize the difficulties which may be met if an attempt is made to remove a septum from a uterus not recently pregnant (Fig. 1). The septum is almost as thick as the uterine wall. If an attempt were made to remove it as it appears here there would be considerable difficulty and danger of doing much damage to the uterus. Because of the danger involved in removal of this thick septum the procedure in the two cases reported here was decided upon.

CASE 1.—Mrs. K. was first examined at my office in February, 1923. She was then four months pregnant. A vaginal examination revealed two vaginas and two cervices. The pregnancy was in the right side. At twenty-four weeks she miscarried. The vaginal septum only was removed at that time. During the early part of this pregnancy there was hyperemesis. There was no bleeding during pregnancy, or hemorrhage at time of the delivery.

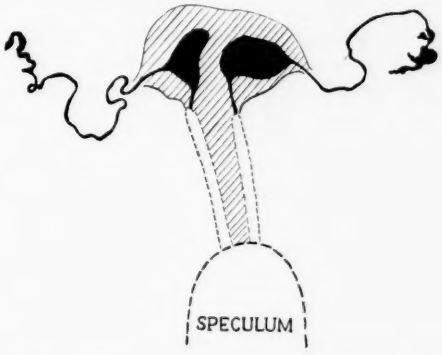

Fig. 1.—Diagram of a lipiodol injection showing a uterus septus. (From Davis *Obstetrics and Gynecology.*)

Two years later there was a second conception. At the sixteenth week the patient developed an acute appendicitis. At that time an appendectomy was done and the uterus sufficiently exposed to see that the fundus was almost normal in shape. The left tubal attachment appeared lower than the right. Below the attachment of the left tube the uterus bulged out and as a result was asymmetrical. The fundus had no separation and the uterus appeared to be about sixteen weeks pregnant. The pregnancy was now on the right side, as shown in Fig. 2. The recovery from the appendectomy was uneventful. Again at the sixth month she miscarried. Immediately after delivery of the placenta and membranes, an intrauterine examination revealed a complete separation of the uterus into two parts. The left side would admit the gloved hand, the right admitted two fingers. The right cavity as well as the os was much smaller.

Having learned that there was no depression of the fundus at the time of the appendectomy, the following procedure was carried out. Two curved stomach clamps were introduced into the cavity of the uterus, one grasping the septum posteriorly, the other anteriorly, so as to conform to the curvature of the inside of the uterine walls (Fig. 3). The septum was removed almost completely with scissors. The

Fig. 2.—Diagrammatic cross-section of a pregnant uterus septus.

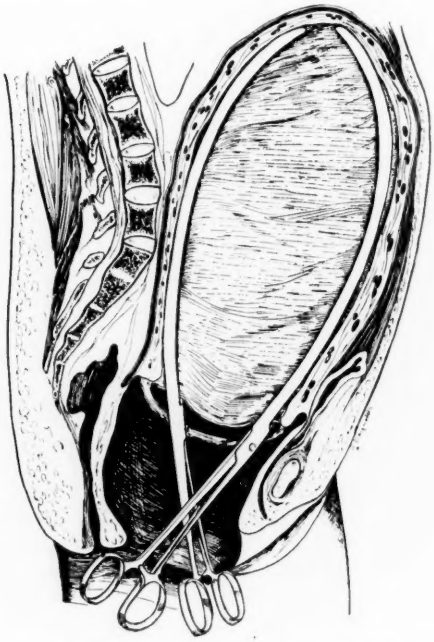

Fig. 3.—Showing application of clamps to the septum before removal.

clamps were left in place twenty-four hours to control hemorrhage. Stomach clamps give satisfactory hemostasis but do not devitalize the tissue; therefore the chances of sepsis should be less than when a crushing clamp is used.

Convalescence was uneventful.

One year later pregnancy again occurred. The uterus seemed symmetrical throughout the pregnancy. Parturition took place at term. The baby lived. The con-

Fig. 4.—Diagram of pregnant bicornate uterus septus.

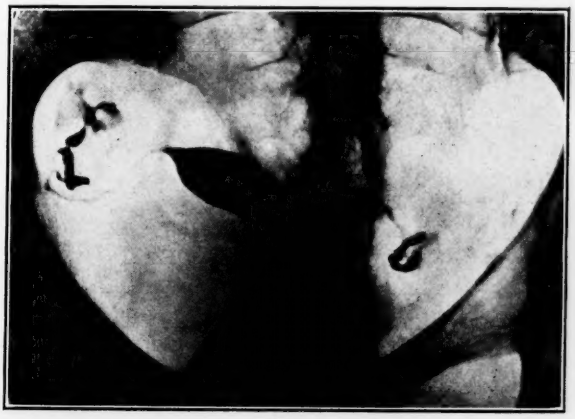

Fig. 5.—Lipiodol x-ray of bicornate uterus six weeks after removal of septum.

valescence was uneventful. Pregnancy and parturition at term again took place two years later. The baby lived. Both babies are normal.

CASE 2.—Mrs. D., aged twenty-six, history of previous illness negative, except for three vaginal operations, which evidently were for removal of a vaginal septum. She aborted eight years ago at the tenth week. Five years ago (Aug. 19, 1930) she had a miscarriage at about the eighteenth week. There was slight uterine bleeding most of the last month. The pregnancy was in the right horn (Fig. 4). At

the time of the miscarriage a vaginal examination revealed a septum in the uterus extending down to the external os. The septum was removed by the same procedure as described above. Recovery was uneventful. The accompanying lipiodol x-ray was taken eight months after the removal of the septum (Fig. 5). Aug. 19, 1934, she gave birth to a full-term baby. She had some spotting during the first five months of pregnancy. The labor and recovery were uneventful. The baby is alive and normal.

A section of neither septum was examined microscopically for muscle tissue. The fact that there is a tendency toward hemorrhage would suggest a lack of muscle tissue, and a preponderance of endometrium in the septum. Furthermore, if the septum was composed of a layer of muscle tissue in proportion to the thickness of the external uterine wall, there should be enough contractile power in it to prevent hemorrhage at time of delivery. On the other hand, if there were muscle fibers in the septum, they would be a continuation of the fibers beginning at the cornu and extending down into the septum. After removal of a septum composed of muscle tissue the contractions of the uterus might be disturbed. The fact that there was no disturbance in the contractions of the uterus in either of the cases reported, would suggest there was little or no muscle tissue in the septum.

It would seem logical to assume that developmental errors in the uterine musculature may be the cause for such dystocias as Bandl's ring, and other disturbances of the normal function of the uterus during labor.

I wish to thank Dr. Sage for permitting me to remove the septum on Case 2, and also for the use of the lipiodol x-ray on this patient.

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1530 Medical Arts Building

DISCUSSION

DR. A. G. POHLMAN, Omaha, Neb.—The development of the female sex ducts is contrary to the general embryologic rule governing such developments on three counts: first, the duct is not structurally associated and continuous with the gland proper; second, the duct does not arise by a surface invagination but is differentiated out from above down and makes secondary contact with the surface upon which it opens; and third, a selective influence through the gonad determines whether or not the continued development of the duct shall take place.

The persistence of the double müllerian fundament and the variations in the degree of the fusion were illustrated by the essayist. It so happens that the mesenchyme condensation about the double duct takes place at an earlier stage than the fusion of the double lumen. Accordingly most of these uterine septa should contain little muscle tissue and the normal functional relation of uterine muscle to endometrium would be wanting.

DR. E. LEE DORSETT, ST. LOUIS, MO.—I feel that these conditions are somewhat more common than we expect. I have had six such cases, two of which were diagnosed as fibroids before operation. We found a double uterus when we operated. The third one had a fibroid in one of the horns. Two patients were pregnant and required cesarean section after prolonged labors, due to the fact that there was a double cervix and one cervix interfered with the dilatation of the other. The sixth case was found only upon postpartum examination. The patient came in in advanced second stage and was delivered by an interne. On postpartum examination at discharge they found a septum with a double uterus. The patient delivered perfectly normally.

In regard to the bleeding during pregnancy, I think we can explain that as due to the fact that one horn has a decidua present and the bleeding comes from that, on the same principle that we get delayed bleeding time.

DR. SAMUEL F. ABRAMS, ST. LOUIS, MO.—My experience is limited to three cases of double uterus. All three patients had been delivered of babies spontaneously. One woman had a breech delivery and on checking up later I found she had a septum and a double uterus. The other patients I sent to the clinic. One patient had had three normal deliveries when we found this double uterus and septum. The third patient came into the hospital bleeding and the resident curetted her with a diagnosis of an incomplete abortion. After he began his curettage he discovered a submucous myoma but did not find the septum. I found a vaginal septum with one nulliparous cervix and one multiparous cervix. This woman had had three pregnancies, apparently all in the same uterus. We did a vaginal hysterectomy, and there were submucous myomas in each uterus, each the size of a walnut. She had no history of difficulty in labor.

DR. LUIKART (closing).—The discussion has brought out very clearly that in a double uterus it is not unusual for pregnancy to go to term and deliver oftentimes without great difficulty, and occasionally, as has been said, the condition has not been recognized. With a septate uterus where the fundus is comparatively normal and there is not much notching, the situation is quite different because as stated in my report, the other half of the uterus is not available for expansion of the uterine cavity.

PREMATURE SEPARATION OF THE PLACENTA AND CIRCULATORY COLLAPSE ASSOCIATED WITH PERICARDIAL EFFUSION*

HARRY EVANS HARVEY, M.D., M.SC.(MED.), F.A.C.S., LINCOLN, NEB.

PREMATURE separation of the placenta has been more commonly regarded as due to systemic disturbance than to mechanical factors. The following case is considered worthy of record because of the unusual sequence of events terminating in the death of the patient, and because of the light which it throws on increased venous pressure as one causal factor in premature detachment of the placenta.

Mrs. R. L., aged sixteen years, para i, was first seen when admitted to St. Elizabeth's Hospital on March 8, 1934, in the thirty-sixth week of pregnancy. The complaint was sudden vaginal bleeding accompanied only by a dull aching abdominal pain beginning about two hours before admission.

The prenatal period had been normal except for recent shortness of breath on exertion. About four weeks before, on her only prenatal examination at the city

*Read at the Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists, held at Omaha, Neb., October 10 to 12, 1935.

clinic, the Wassermann test was negative, the blood pressure was 132/84, and the urine showed a trace of albumin. There was nothing of note in the personal, family, or past history except that the patient had had mild scarlet fever a short time before the date of conception.

On examination the patient appeared to be in distress. She was warm, the color was good, pulse 100, of good quality, blood pressure 122/82. The area of heart dullness was broad, the apex beat was not felt. The heart was regular, no murmurs; the sounds were distant but clear and of a ringing quality similar to that of the fetal heart sounds. The size of the uterus corresponded to the period of gestation. There was tenderness and muscle rigidity over the right lower two-thirds of the abdomen. The uterine muscle was in constant contraction. The fetal heart was heard in the midline below the navel but position could not be determined by abdominal palpation except to note that the head was at the pelvic inlet. The cervix was soft but not effaced or dilated. There was a sense of bogginess to the right of the cervix and very slight vaginal bleeding. A diagnosis was made of premature separation of the placenta, and after consultation cesarean section was elected as the procedure of choice.

On opening the abdomen the uterine veins were found greatly dilated. The uterine cavity was opened by a classical incision and a living male child weighing 7 pounds 5 ounces (3,323 gm.) was delivered. The placenta was elongated, extending over the lower two-thirds of the right lateral wall of the uterus with the insertion of the cord at the upper margin. The lower half of the placenta was separated from the uterine wall by 200 to 300 c.c. of dark and unclotted blood. The wall of the uterus was not infiltrated, and it contracted firmly with but little blood loss. As the wound was being closed the pulse became fast and thready, then imperceptible. Attempts at resuscitation were unsuccessful.

Necropsy: (Significant findings as reported by Dr. J. Marshall Neely.) There was no evidence of exsanguination. The diaphragm was at the level of the third interspace on the right and the fourth on the left. The liver border extended below the costal margin. The pericardium was parchment-like in character with definite thickening and contained over 600 c.c. of slightly blood-tinged fluid. The transverse diameter of the heart was 9 cm. The organ was not remarkable in appearance except that the right ventricle was totally collapsed with the lateral wall in contact with the interventricular septum.

On microscopic examination there was fibroblastic and polyblastic proliferation beneath the epicardium and of the pericardium, apparently not of recent origin. Although no Aschoff bodies were found, the reaction was thought to represent rheumatic type of histology. Grossly the kidneys were normal but microscopically there was evidence of focal nephritis.

DISCUSSION

While no report of a similar case has been found in the literature, many are recorded in which some parallel phases have been observed and studied. The relative infrequency of the diagnosis of pericardial effusion during life has been noted by Camp and White,[1] who found that in 129 cases with an effusion of 100 c.c. or more only six were correctly diagnosed and in no instance was the diagnosis made in the presence of less than 500 c.c. The widening of the area of heart dullness due to the rotation of the heart is regarded as a normal finding late in pregnancy.[2, 3]

Except for observations in pericardial effusion and adhesions, the works on physiology offer little information on changes in venous pressure during effort or in the presence of vascular or systemic disease. Pericardial effusion has been commonly observed following scarlet fever. Williamson and Ets[4] and others[5] conclude from clinical and experimental observations that as the intrapericardial pressure is increased there is a general rise in the venous pressure and lowering of the arterial pressure.

A traditional method of inducing termination of an unwanted pregnancy among certain European peasants is by the lifting and moving of sacked grain. Premature foaling has been observed in mares after violent straining efforts in drawing a load. There is a certain difference in the uteroplacental attachment in women and in mares but in initiating the effort both expand the chest, close the glottis, fix the diaphragm and contract the abdominal muscles, producing an increased abdominal pressure and venous engorgement.

Morse[6] has produced infiltration of the myometrium and premature separation of the placenta in rabbits by ligating the veins and suggests that torsion of the uterus or any other obstruction to the return flow may produce a characteristic picture of premature separation of a normally implanted placenta. Polak[7] has observed premature separation of the placenta in cases in which a marked torsion of the uterus was present and concludes that many cases of separation of the placenta have an "apoplectic origin in torsion of the uterus." It seems possible that the increase in venous pressure which accompanies pericardial effusion might produce separation of the placenta in the same manner as obstruction of the veins by torsion.

Sudden death due to release of intraabdominal pressure with accumulation of blood in the great veins has been observed following rapid removal of ascites or large cysts. And Williamson and Ets[4] also noted in pericardial effusion that at a certain critical point the fall in arterial pressure is sudden and circulation ceases, and the patient "dies as a result of the pressure of the exudate mechanically shutting off the great veins." Bay, Gordon and Adams[8] noted experimentally that elevation of the intrapericardial pressure beyond a certain point produced a marked fall in the arterial pressure. After experimental occlusion of the vena cava, they observed blood pressure curves resembling those noted in pericardial effusion experiments. Reducing the intraabdominal pressure by abdominal delivery would be followed by lowered pressure within the great veins with effects on the filling of the heart parallel to what would occur on ligation of the vena cava and, relatively, the same as increasing the intrapericardial pressure.

SUMMARY

A case is reported in which the sequence of events is believed to have been as follows: Scarlet fever followed by pericardial effusion; increase in the pressure within the great veins accompanying the increased intrapericardial pressure; passive congestion of the liver; and finally, rupture of the venous sinuses in the placental site due to relative obstruction of the venous return. On sudden release of the intraabdominal pressure by abdominal delivery the pressure within the inferior vena cava fell below the intrapericardial pressure and the heart was no longer able to fill.

It appears that a marked and prolonged increased venous pressure may produce premature detachment of the placenta and that the relation between increased venous pressure and premature separation of the placenta warrants further study.

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809 Sharp Building

THE ACTION OF OVARIAN FOLLICULAR HORMONE IN THE MENOPAUSE, AS INDICATED BY VAGINAL SMEARS*

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NEW YORK, N. Y.

(From the Departments of Anatomy and Medicine, Cornell University Medical College, and the New York Hospital)

IN A PREVIOUS report[11] we gave a brief account of our observations on the effect of the ovarian follicular hormone upon women in the menopausal state, using as a criterion the morphologic changes occurring in the vaginal secretion. Adequate treatment with this hormone induced a series of progressive changes in the vaginal fluid which culminated in a type of vaginal smear comparable to that observed in normal women during the high follicular (copulative) phase of the menstrual cycle.[9] At the same time, there occurred a gradual subsidence of the menopausal symptoms corresponding closely to the progressive improvement in the smear. A simple and exact method was thus made available for evaluating the effects of this hormone as well as for regulating its administration in any individual case.

We have since extended these studies to include approximately fifty women with the menopausal syndrome, either natural or following surgical procedures or irradiation. A complete report of our findings will be given in another paper. Our present purpose is to describe in detail the sequence of fundamental changes which take place in the vaginal secretion during the administration of the ovarian follicular hormone in two representative cases. This should permit the more general use of the method in the study and treatment of menopausal conditions.

METHODS AND MATERIAL

The technic followed in taking and staining smears is the one previously described by Papanicolaou.[9] A number of control smears were taken prior to any treatment, to establish the individual smear type. During the periods of intensive study, smears were taken daily. The patients were supplied with a glass pipette, a number of dated slides and a jar containing equal parts of 95 per cent alcohol and ether. Paper clips were attached to the slides to prevent rubbing while in the jar. The subjects were instructed to prepare their own smears and to drop the slides immediately into the alcohol-ether mixture, where they were kept until brought to the laboratory. They were stained with hematoxylin, eosin and waterblue. Drying of the smears was carefully avoided. While daily smears were of great value for the purposes of

*This work has been aided by grants from the Committee for Research on Sex Problems, of the National Research Council, and the Council on Therapeutics of the American Medical Association.

intensive study, a smear taken at the time of the weekly clinic visit was found adequate for the ordinary routine treatment. The examination of the smear served as a guide for further treatment.

Two ovarian follicular hormone preparations were chiefly used.* One was the *ketohydroxyestrin*[5] in the form of amniotin, in oil solutions, for hypodermic or oral use. The other was the *dihydrofollicular hormone*[13] first synthesized from the ketohydroxy form, and later found naturally occurring in the urine of pregnant mares and the ovaries of sows. The latter preparation was employed as the benzoated form, available as progynon-B for hypodermic use, and the unconjugated progynon for oral administration. The injections were given intramuscularly deep in the gluteal region. The oral preparations were taken on an empty stomach.

THE MENOPAUSAL TYPE OF SMEAR

The organs of the female genital tract undergo considerable atrophy after the onset of menopause. This is more pronounced when the menopause is the result of a complete ovariectomy. The vagina and its epithelium participate in this atrophy. As a result, the vaginal secretion is altered, and characteristic changes in the vaginal smear take place.

Those cases in which atrophy is advanced are marked by the presence of numerous compact, round or oval cells which stain deeply and possess rather large round or oval, well-preserved nuclei (Fig. 2). These cells are derived from the deeper layers of the vaginal epithelium and are rarely seen during the normal menstrual cycle. Superficial cells are also to be found in varying numbers. Their relative scarcity and the abundance of deep cells are the result of the thinning of the epithelium and the absence of a well-developed superficial zone.

Leucocytes are also very numerous in this type of smear, as the result of their unhampered migration through the thin epithelial wall.

Erythrocytes are frequently found in varying numbers. Their presence may often be overlooked because of decolorization or fragmentation. Sometimes the presence of blood is evidenced solely by fibrination without formed elements. Such fibrin formation may be easily confused with bacterial agglutinations. The frequent appearance of erythrocytes in the menopausal smear is quite significant. It points to a small but constant loss of blood and constitutes a distinct type of bleeding which might be designated as *menopausal atrophic bleeding.*

When the atrophy of the genital tract is less pronounced, the smears display great variability. The numbers of deep cells may vary from great abundance to almost complete absence (Fig. 17). The superficial cells are more prominent. Their general characteristics are the

*We are indebted to Dr. J. J. Durrett of E. R. Squibb and Sons and to Dr. E. Schwenk of the Schering Corporation, for their generous supply of amniotin and progynon-B, respectively.

absence of uniformity and sharpness in outline and structure, and their tendency to form compact irregular clumps. The cells are frequently folded and shrunken. The cytoplasm is poorly preserved and the nuclei are generally irregularly shaped. The size of the nucleus is rather large, though cells with small nuclei may often be present.

In addition to the cellular elements, there are several other features of the smear which are of interest.

There is, as a rule, a moderate amount of mucus. It is rarely abundant, and occasionally very scant.

The bacterial flora is generally rich, giving a "dirty" appearance to the smear. There is a great variety of forms. Of particular importance is a bacillus, probably identical with the *Bacillus vaginalis* of Döderlein. Its presence is associated with a cytolysis of the cellular elements, the nuclei of which may be seen free in the smear. The fragmentation of the cells is probably due to the penetration of the bacteria into the superficial layers of the vaginal wall. Smears of this type are very characteristic. *Trichomonas vaginalis* has been found with fair frequency.

The absence of sharp outlines, the irregularity in the shape of the cells, and the tendency to form compact irregular clumps after the menopause, as well as the increase in bacteria and the dirty and smudgy appearance of the smears, may be chiefly attributed to two factors: first, the prevailing atrophy of the epithelial wall of the vagina and the lack of a superficial cornified zone; second, the decrease in the activity of the desquamatory and secretory processes, with the ensuing prolonged retention of the cellular detritus within the lumen of the vagina.

Another factor in the production of variability in the postmenopausal smear is the occasional appearance of rhythmic changes.[10] We have observed such cyclic changes in a number of patients who were under prolonged observation prior to the treatment. Spontaneous change to the follicular type of smear took place with subsequent regression to the original type.

No matter what the original type of smear, the final changes induced by treatment are extremely uniform. An entirely different smear makes its appearance as a result of sustained adequate treatment with ovarian follicular hormone. This is characterized by the disappearance of leucocytes and erythrocytes, and by the replacement of all other cells by large, flat, well-outlined cells, many of them cornified, with small pyknotic nuclei. These cells appear isolated or in small groups. The smear takes on a clean, clear-cut appearance, and permits a ready differentiation from the original type (Fig. 2).

CHANGES IN THE VAGINAL SMEAR DURING THE ADMINISTRATION OF OVARIAN FOLLICULAR HORMONE

The series of progressive changes which take place in the vaginal secretion during the administration of ovarian follicular hormone will be illustrated by two representative cases which were studied over long periods.

CASE 1.—E. G.,* aged thirty-eight, single, white. Surgical menopause. Menstrual history: Onset at seventeen, thirty-one-day interval, duration of flow three days,

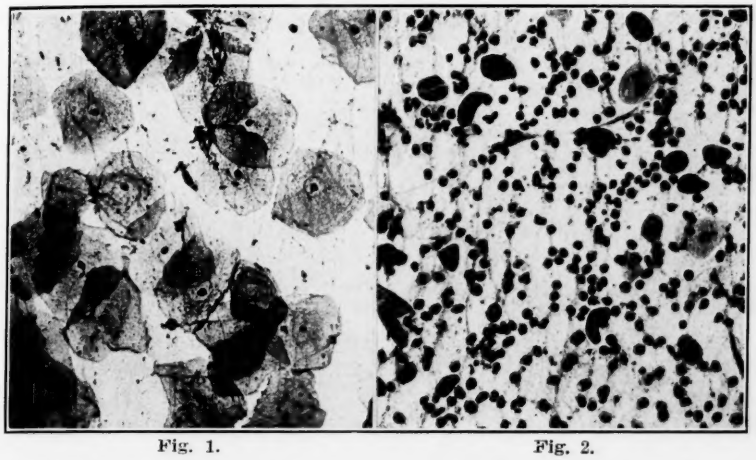

Fig. 1. Fig. 2.

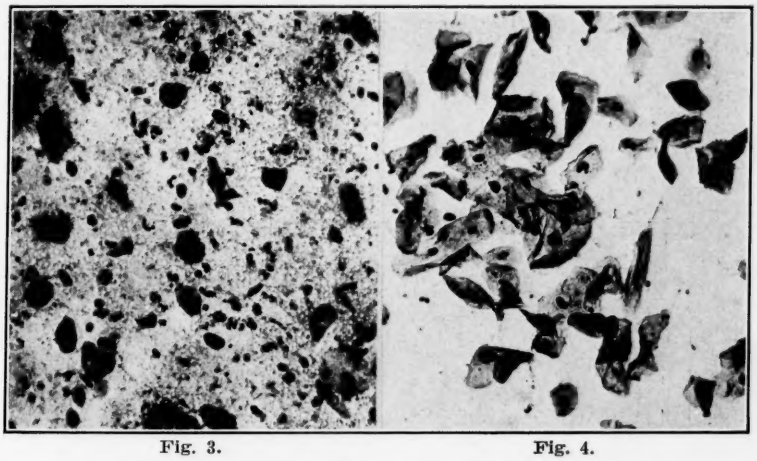

Fig. 3. Fig. 4.

PLATE I.†—PHOTOMICROGRAPHS OF HUMAN VAGINAL SMEARS.

Fig. 1.—Follicular (copulative) phase of a normal woman at the 11th day of the menstrual cycle. Note leucopenia and prevalence of large flat cells with pyknotic nuclei, either isolated or in small groups.

Fig. 2.—Case E. G. Surgical menopause before treatment. Note abundance of leucocytes and prevalence of round or oval deep cells. Some erythrocytes are present.

Fig. 3.—Case E. G. During treatment with O.F.H. Note abundance of mucous secretion as an early effect of treatment.

Fig. 4.—Case E. G. Shows disappearance of leucocytes and erythrocytes, and clearing of smear on further treatment. Deep and elongate cells prevailing.

*A summary of this case is given in Table I.

†All photomicrographs have been equally magnified. Oc. 10; Obj. 20; Bellows 69.

TABLE I. SUMMARY OF CASE 1

DATE OF SMEAR	2/14/35	2/20/35	2/21/35	2/27/35	3/4/35	3/16/35	3/31/35	4/25/35	5/1/35	5/29/35	6/26/35
FIGURE NO.	2	3	4	5	6	7	8	9	10	11	12
Amount of hormone given in interval preceding each smear. No. of rat units and route	Before treatment	Amniotin 1,000 (hypo)	Amniotin 500 (hypo)	Amniotin 2,750 (hypo)	Amniotin 3,000 (hypo)	Amniotin 750 (hypo) 14,000 (oral)	No treatment for 18 days	Amniotin 4,000 (hypo)	Amniotin 4,000 (hypo)	No treatment for 29 days	Progynon-B 70,000 (hypo)
Grand total—rat units		1,000 (hypo)	1,500 (hypo)	4,250 (hypo)	7,250 (hypo)	8,000 (hypo) 14,000 (oral)		4,000 (hypo)	8,000 (hypo)		70,000 (hypo)
Period of treatment-days	0	2	3	7	12	24		25	30		29
Last treatment prior to smear		2/20	2/21	2/27	3/4	3/13	3/13	4/25	4/30	4/30	6/24
Mucus	Moderate	Excessive	Greatly diminished	Moderate diffused	Moderate diffused	Scant	Moderate	Scant	Considerable diffused	Scant	Scant
Leucocytes	Very numerous	Numerous	Few	Few	Leucopenia	Leucopenia	Numerous	Leucopenia	Leucopenia	Very numerous	Leucopenia
Erythrocytes	Numerous	Numerous	Rare	None	None	None	None R.B.C. present 3/19 and 3/20	None	None	None R.B.C. present 5/7, 9, 12, 14, 16	None
Clearness of smear	Hazy	Hazy	Clearer	Fairly clear	Clear	Clear	Hazy	Clear	Clear	Hazy	Clear
Deep cells	Numerous	Numerous	Less numerous	Rare	None	None	Numerous	None	None	Numerous	None

TABLE I—CONT'D

Superficial cells	Moderate number	Unchanged	Many elongate forms	Flatter, larger with smaller nuclei	Most are flat with small nuclei	Most are elongate and elliptic	Folded with poor outlines	Folded. Elliptic with sharper outlines. Small nuclei prevailing	Most are flat with small nuclei	Less numerous. Most with large nuclei	Large. Flat with small nuclei
Grouping of cells	Moderate	Moderate	Moderate clumping	Cells more discrete	Cells isolated or in small groups	Denser groups	Moderate clumping	Denser groups	Cells isolated or in small groups	Moderate	Cells isolated or in small groups
Typical cornified cells	None	None	None	Few appearing	Many	Many still present	None	None	Many	None	Many
Extent of effect	—	Slight	Moderate	Advanced	Complete	Slight regression	Marked regression	Moderate	Complete	Regression close to original	Complete
Symptoms	Severe	Slight improvement	Further improvement	Continued improvement	Complete relief	Complete relief	Quite severe	Considerable improvement	Complete relief	Original intensity	Complete relief
Vaginal smear types	Menopausal atrophic	Mucus	Leucopenic with deep and elongate cells	Leucopenic early follicular	Leucopenic follicular	Leucopenic grouped	Menopausal intermediate	Leucopenic grouped	Leucopenic follicular	Menopausal. Atrophic	Leucopenic follicular
Vaginal epithelium									Fig. 13. Hypertrophic. Well developed superficial cornified zone	Fig. 14. Atrophic menopausal type. Poorly developed superficial zone	Fig. 15. Hypertrophic. Well-developed superficial cornified zone

generally scant. Dysmenorrhea for three years prior to operation in 1932, at which bilateral cystic ovaries were removed with the exception of small remnants. No menstruation following operation. Menopausal symptoms set in three weeks after operation and have persisted: hot flushes ++++, nervousness and irritability +++, depression ++, asthenia +++, insomnia ++. Libido never great, now completely absent. Previous health good except for catarrhal deafness. Blood pressure 125/80.

Control Smear.—Vaginal smears taken before treatment (Fig. 2) showed a large number of leucocytes and a good many well-preserved erythrocytes. There were numerous typical deep cells together with other atypical squamous forms. There were no cornified cells. A small amount of mucus was present.

Treatment.—On February 19-20, 500 R.U. of amniotin in oil were given hypodermically each day (totaling 1,000 R.U.). A smear (Fig. 3) was taken about ten hours after the second injection.

A definite change in morphology had already occurred. The most characteristic effect was the excessive secretion of mucus. The epithelial cells were practically unchanged. The leucocytes were somewhat diminished in number, but the erythrocytes were still numerous.

The excessive mucous secretion is one of the most typical evidences of reaction to the administration of the hormone. This might be called the *mucous stage.* It may appear even after the administration of small doses and is frequently accompanied by slight symptomatic improvement.

In this patient, the number of flushes had diminished somewhat on the day the smear was taken.

Treatment.—On February 21, another injection of 500 R.U. of amniotin was given (500 + previous 1,000 = total 1,500 R.U.).

A slide (Fig. 4), taken on February 22, showed an almost complete disappearance of leucocytes and erythrocytes. The mucous secretion had greatly diminished. A definite change in the appearance of the epithelial cells was seen. The round or oval deep cells were less numerous. A large number of the cells had an elongate form which is very characteristic of this stage. The cells were still largely in clumps, with no typical individualization. The nuclei were still large. In general, the smear was clearer, with a diminution in the number of bacteria. This stage might be designated as *leucopenic, with deep and elongate cells.*

Symptomatically, the patient showed some additional improvement with respect to severity and number of flushes.

Treatment.—Further treatment was administered as follows: February 23 through 26, 500 R.U. daily; February 27, 750 R.U. (total, 2,750 + previous 1,500 = 4,250 R.U.).

In the smear (Fig. 5) taken February 27, ten hours after the injection, a further improvement was noticeable. The leucopenia persisted,

and the deeper cells were further diminished in number. Few elongate and some navicular types of cells were seen. The cells were flatter, had sharp outlines, and were becoming discrete.

A new type of cell made its appearance and began to predominate. It was flat, irregularly outlined, frequently polygonal or rounded with a small pyknotic nucleus sometimes surrounded by a small vacuole. The cytoplasm often contained small granules. A good many of the cells were elliptic in form.

A certain amount of mucus was present diffusely throughout the smear. The number of bacteria was still fairly large and gave a dirty appearance to the slide. This state might be designated as *leucopenic early follicular.*

Further symptomatic improvement with respect to number of flushes and increased well-being was reported by the patient.

Treatment.—Seven hundred fifty R.U. per day were given on February 28, March 1, 2, 4. (Total = 3,000 + previous 4,250 = 7,250 R.U.)

The next slide (Fig. 6), was taken on March 4, ten hours after the last injection. A decided improvement had taken place. The cells had gradually changed into the cornified flat type with pyknotic nuclei. The deep cells entirely disappeared as had the cells with the large nuclei. The smear was much clearer and showed a great decrease in the number of bacteria. Some mucus was present throughout the smear. This stage might be termed the *leucopenic follicular phase,* corresponding to a similar phase occurring during the normal menstrual cycle (Fig. 1). This is the period during which the growing follicles reach their full maturity prior to ovulation.

When this stage is reached with the administration of ovarian follicular hormone, the patient, as a rule, shows optimum symptomatic improvement. Nor, with increasing dosage, is the smear changed further. We therefore regard this as the optimum stage in the management of the patient.

An effort was now made to maintain this condition by the use of the hormone by mouth.

Treatment.—On March 6, 250 R.U. of amniotin were given by hypo; on March 7, and 8, 250 R.U. by hypo plus 2,000 R.U. orally; from March 9 through 13, 2,000 R.U. daily orally (total 750 hypo + 14,000 oral + 7,250 hypo previously = 8,000 R.U. hypo + 14,000 R.U. oral).

The next slide (Fig. 7) illustrates the condition of the smear on March 16. There was a continued leucopenia, but a regression in cell type. Cells with small nuclei were still prevailing. They were, however, elliptical elongate, or navicular, tended to fold and form denser clumps. A smear of this type might be designated as *leucopenic grouped.* It should be considered as indicating some regression in the general composition of the smear. Symptomatic relief, however, was still maintained.

Treatment.—No further treatment was administered until April 1.

The smears underwent regressive changes reversing the stages through which they had passed during the treatment.

Of particular interest was the *appearance of erythrocytes* on March 19 and 20 (sixth and seventh days after cessation of treatment). The type of the smear during these two days was the *leucopenic grouped*, with leucopenia and heavily grouped small-nucleated cells. Papanicolaou[10] described a similar type of smear, associated with bleeding, at the end of the follicular phase in the postmenopausal cycle. It closely corresponds to the ovulatory (midmenstrual) bleeding of the normal cycle.[9]

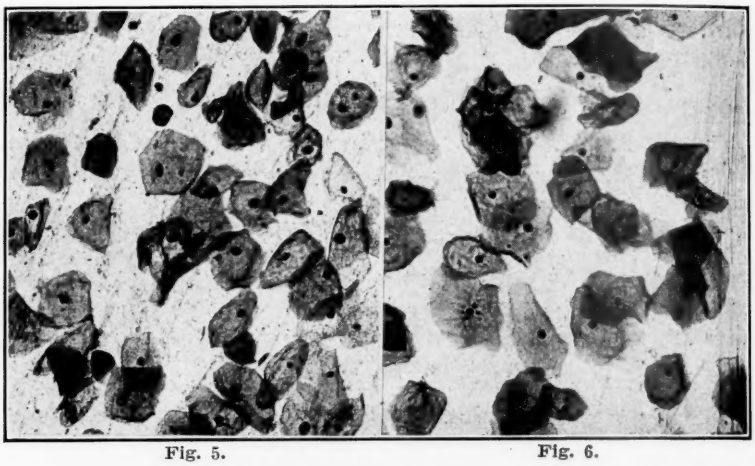

Fig. 5. Fig. 6.

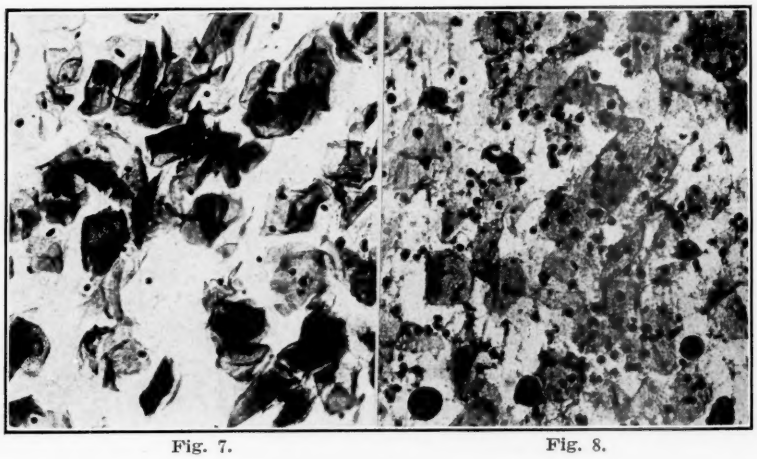

Fig. 7. Fig. 8.

PLATE II.—PHOTOMICROGRAPHS OF HUMAN VAGINAL SMEARS.

Fig. 5.—Case E. G. Early follicular phase induced by further treatment. Note leucopenia and appearance of flat, larger cells with pyknotic nuclei.

Fig. 6.—Case E. G. Typical follicular phase induced by further treatment. Note leucopenia and prevalence of flat cells with pyknotic nuclei.

Fig. 7.—Case E. G. Regressive grouped type of smear induced by insufficient oral treatment. Leucopenia is still persisting.

Fig. 8.—Case E. G. Further regression on discontinuation of treatment. Note reappearance of leucocytes and deep cells.

By March 31 (eighteen days after the last treatment), the smear (Fig. 8) had reverted to a type with numerous deep cells, many leucocytes and a complete absence of large flat cornified elements.

Symptomatically, the beneficial effects of the medication persisted for approximately a week or ten days after treatment was stopped. After March 21 there followed a gradual return of the symptoms, not, however, to their original intensity.

Treatment.—On April 1, treatment was resumed as follows: 250 R.U. amniotin in oil by hypo on the following days: April 1, 4, 6, 9, 10, 11, 12, 13, 15, 16, 17, 18, 20, 23, 24, 25 (a total of 4,000 R.U. over a period of 25 days).

The smears again showed the same gradual change as before, but did not progress beyond the stage shown in Fig. 9 which was taken on April 25. This corresponds closely to Fig. 7, indicating an incomplete reaction.

Treatment.—The dose was then increased to 1,000 R.U. and given on the following days: April 26, 27, 29, 30 (4,000 R.U. over five days + 4,000 R.U. previous 25 days = 8,000 R.U. in 30 days).

The result was a radical change in the smear which on May 1 (Fig. 10) showed a typical follicular reaction as described above. A disappearance of the patient's distressing symptoms occurred with this last change.

At the time of this smear (May 11), a biopsy of the vaginal wall was taken (Fig. 13). The epithelium was high with an orderly arrangement of the cells throughout.* The superficial cells showed cornification and small pyknotic nuclei. The germinative or basal zone was well differentiated into an inner and outer zone. An enlargement of the nuclei, particularly of the outer basal zone, was noticeable. Some mitotic figures were present. This microscopic picture corresponds to the type which we have observed in a normal woman during the follicular phase.[12]

Treatment.—Treatment was stopped for twenty-nine days (from May 1 to 29).

Again, a gradual regression to the original type of smear took place, in stages similar to the previous withdrawal period, as well as a return of all symptoms in their original intensity. Again, *slight microscopic bleeding* appeared on May 7, 9, 12, 14, and 16 (6, 8, 11, 13, and 15 days after the cessation of therapy). The final smear of May 29 (Fig. 11) was, except for the absence of erythrocytes, similar to the original smear (Fig. 2). On the same date, a vaginal biopsy (Fig. 14) showed a decrease in height of the epithelial wall, and an absence of a well-defined outer basal zone. The orderly superficial zone of cornified cells with small pyknotic nuclei was replaced by a narrower zone consisting of smaller, more compact cells with larger nuclei.

*This paper had been completed when the study of M. E. Davis on the "Treatment of Senile Vaginitis with Ovarian Follicular Hormone" *(Surgery, Gynecology, and Obstetrics* **61**: No. 5, 1935) appeared. The restoration of the vaginal epithelium on the administration of ovarian follicular hormone is clearly demonstrated.

Our next procedure was to study the effects of larger doses of the hormone spaced at wider intervals, as compared with the frequent (usually daily) maintenance doses as described above. For this experiment progynon-B was used.

Treatment.—Injections of 10,000 R.U. were given on the following days, at approximately four-day intervals: May 29, June 3, 7, 12, 17, 20, 24.

On May 31, two days after the first injection, the vaginal smears showed a beginning transition of the cell forms from the atrophic phase, and a virtual disappearance of leucocytes and erythrocytes. On the evening of June 3, following the second injection of 10,000

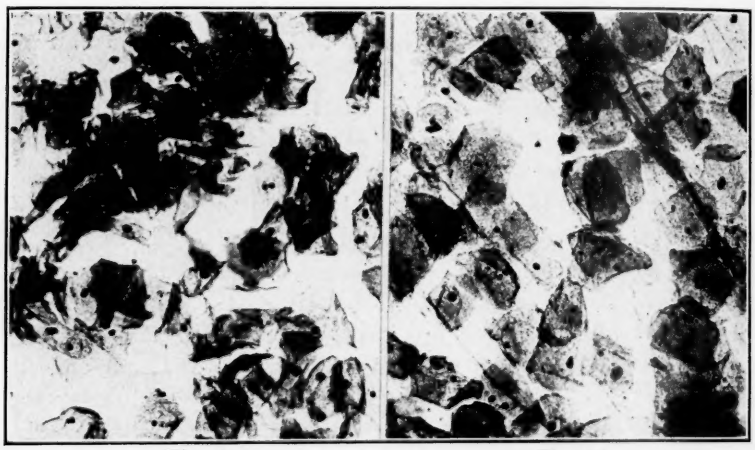

Fig. 9. Fig. 10.

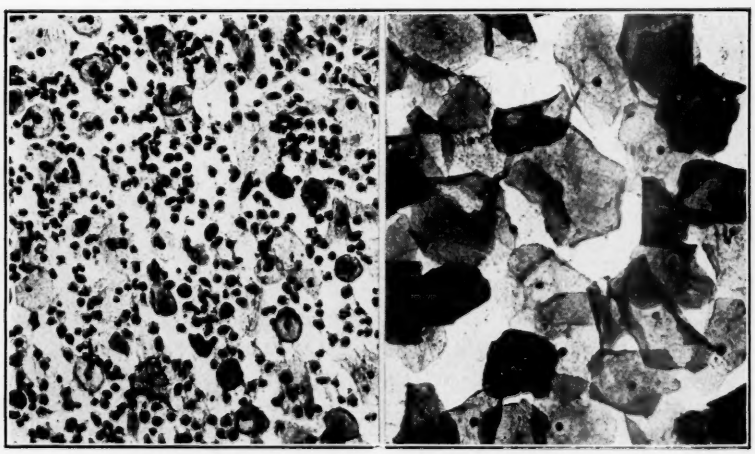

Fig. 11. Fig. 12.

PLATE III.—PHOTOMICROGRAPHS OF HUMAN VAGINAL SMEARS.

Fig. 9.—Case E. G. Leucopenic grouped type after resumption of treatment.
Fig. 10.—Case E. G. Typical follicular smear type induced by further treatment.
Fig. 11.—Case E. G. Almost complete regression to original type after discontinuation of treatment. Note return of many leucocytes and deep cells.
Fig. 12.—Case E. G. Follicular phase following resumption of treatment.

R.U., cells of the follicular type with small pyknotic nuclei began to predominate. By June 7, after the third injection, further improvement to the almost complete follicular phase had taken place. A total of 30,000 R.U. of dihydrofollicular hormone, given over nine days, was

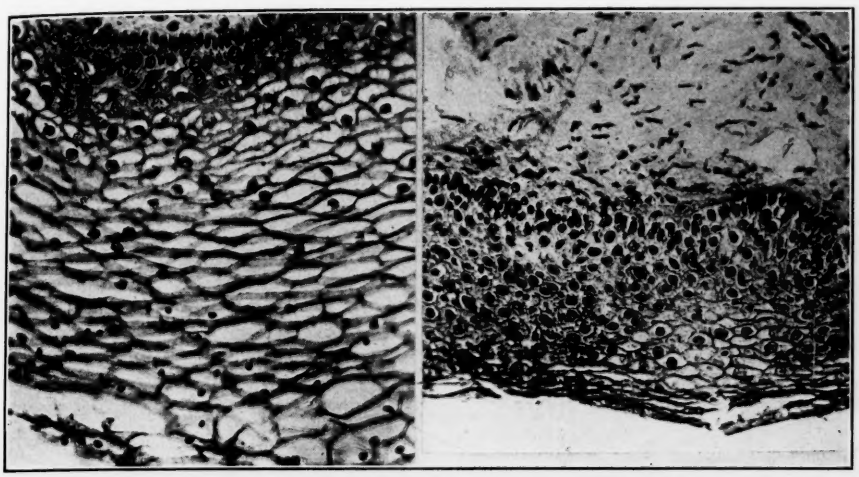

Fig. 13. Fig. 14.

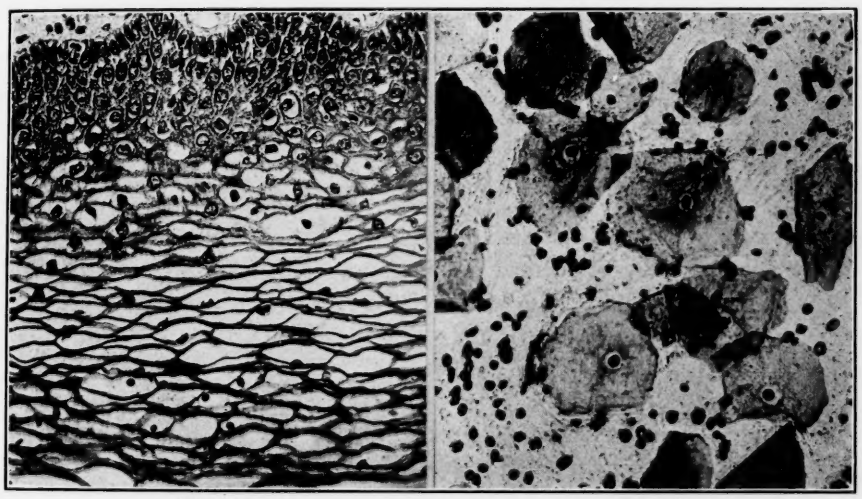

Fig. 15. Fig. 16.

PLATE IV.—PHOTOMICROGRAPHS OF CROSS-SECTIONS OF HUMAN VAGINAL EPITHELIUM.

Fig. 13.—Case E. G. Hypertrophy of vaginal epithelium induced by treatment. Note regularity in structure and superficial cornified zone with pyknotic nuclei. Fig. 10 illustrates corresponding smear.

Fig. 14.—Case E. G. Regression of vaginal epithelium after discontinuation of treatment. Superficial cornified zone has disappeared. Fig. 11 illustrates corresponding smear.

Fig. 15.—Case E. G. Hypertrophy of vaginal epithelium after resumption of treatment. Note reappearance of superficial cornified zone and orderly structure. Fig. 12 illustrates corresponding smear.

Fig. 16.—Case M. B. Smear. Withdrawal bleeding two days after discontinuation of treatment. Note persistence of leucopenia and of flat cells with pyknotic nuclei, as in follicular phase.

sufficient to induce this transformation. From then on until June 26, with injections given at the intervals noted above, the smears retained in general this follicular type, with only slight regressive tendencies which were indicated by the grouping of the cells in some of the slides. Fig. 12 shows the smear and Fig. 15 the biopsy of the vaginal epithelium taken on June 26, after 70,000 R.U. had been administered over a period of twenty-nine days. The vaginal smear showed a fairly typical follicular reaction. The biopsy showed a well-defined superficial cornified zone and a good differentiation of the inner and outer basal zones of the vaginal epithelium, as compared with Fig. 14.

The symptoms, which had reappeared in their original intensity, responded extremely well to this regime. By June 3, a definite improvement was reported, and the symptoms had diminished in intensity. By June 7, flushes had decreased from seventeen to four a day and were much milder. There was slight residual nervousness and irritability. The mood had become cheerful and there was much less fatigability. On June 12, fifteen days after the start of treatment, the relief of symptoms was practically complete, the only residual being an occasional mild flush. In this instance, the peak of the smear improvement was reached a few days before the optimum symptomatic state.

It is apparent that the desired effects of ovarian follicular hormone treatment can also be obtained by injections of larger doses given at wider intervals. However, this method of treatment, although more convenient, is less efficient with respect to hormone requirements and symptomatic relief. In this instance, a dose averaging 2,500 R.U. per day was needed to induce and maintain the changes which were achieved by 1,000 R.U., when given daily. This may be explained by the fact that catabolic changes, as indicated by regressive alterations in the smear, appear as early as two to three days after the treatment, even with doses as large as 10,000 R.U. To avoid the waste of the hormone which is very likely associated with the repair of these regressive changes, it would appear desirable that injections be given daily whenever possible.

THE EFFECTS OF ORAL ADMINISTRATION OF OVARIAN FOLLICULAR HORMONE UPON THE VAGINAL SMEAR

In view of the objectivity of the method developed in this study, an opportunity was afforded of throwing additional light on the question of the intestinal absorption of ovarian follicular hormone in human beings, and its relative efficiency as compared with the hypodermic administration.

In the following case, amniotin was administered orally.

CASE 2.—W. G., aged fifty-eight, white, married; menstrual history: onset at thirteen, twenty-one-day cycle, duration three to four days, flow generally scant. At forty-eight, periods became progressively shorter and more profuse and, after three or four months, ceased. No period since. Married at forty-eight. No pregnancies. No operations. General health good, except for menopausal symptoms which set in at fifty-two years and have persisted: flushes +++, asthenia ++, nervousness ++++, depression +, insomnia +, numbness of hands +++, palpitation ++, occasional headaches. General examination essentially negative except for moderate obesity. Blood pressure 122/78. No gynecologic pathology.

Several control smears taken before treatment were uniform. Fig. 17 shows a smear taken May 3, 1935. It was characterized by thick clumps of irregularly shaped cells without sharp outlines. Their nuclei were mixed in character, a few being small, but the majority were of medium size. Typical deep cells were seen in small numbers. Leucocytes were abundant, mostly old and partly degenerated. A good many erythrocytes were present in some of the control smears. Bacteria were abundant, imparting a diffusely dirty appearance to the smear.

Treatment.—On May 10, 11, 12, 2,000 R.U. of amniotin in oil were taken by mouth (total = 6,000 R.U. orally).

The smear illustrated in Fig. 18, was taken on the evening of May 12. It showed definite signs of the early mucous reaction which we have described above (compare Fig. 3). An abundance of mucus was present, giving to the smear a dense appearance.* The cells had sharper outlines and a good many appeared singly throughout the smear instead of in groups. Leucocytes had somewhat decreased in number. Microscopic bleeding was evidenced by considerable fibrination and the presence of fragmented erythrocytic granules. This is seen in the photomicrograph as a dark network. Bacteria were abundant and appeared as lighter granular aggregations throughout the smear.

Symptomatic changes at this time were indefinite.

Treatment.—On May 13, 14, 15, 16, 2,000 R.U. of amniotin in oil by mouth. On May 17, 3,000 R.U. (6,000 R.U. previously + 11,000 R.U. = total 17,000 R.U. orally).

The vaginal smear taken on the evening of May 17 (Fig. 19) showed a disappearance of leucocytes and erythrocytes. The cells were better outlined, mostly elongate and elliptic and massed in dense groups. The nuclei were chiefly of the small pyknotic type. The smear was clearer. However, bacteria were still present in large numbers. The vaginal films were rather dry without much mucus. This reaction is comparable to the one described in the previous case (compare Figs. 7 and 9), and which we have designated as *leucopenic grouped.*

At this time, a definite but partial improvement in symptoms was described by the patient.

Treatment.—May 18, 19, 21, 22, 23—3,000 R.U. amniotin orally. (17,000 R.U. previously + 15,000 = 32,000 total.)

Continued symptomatic improvement occurred but there were no further changes in the smear.

Treatment.—May 24 through 29, 4,000 R.U. amniotin orally daily. May 31 through June 6, 5,000 R.U. amniotin orally daily. June 7 through June 10, 6,000 R.U. per day. June 11 through June 22, 8,000 R.U. per day. (Total: 32,000 previously + 174,000 R.U. = 206,000 R.U. over 43 days.)

*The increase in mucous secretion is often noticeable on gross inspection by the large amount of thick vaginal secretion which adheres to the slide.

During this period, the smear remained almost stationary at the level illustrated by Fig. 19. It was not until June 22, after the patient had received 8,000 R.U. daily for eleven days, that the smear reached the higher level illustrated by Fig. 20. The cells became more discrete and better outlined. Forms, characteristic of the follicular phase, with small pyknotic nuclei predominated. The large dense groups of cells were no longer evident. There was a complete leucopenia and erythrocytes were absent. The smear was much clearer with a considerable decrease in the number of bacteria. A small amount of mucus was present. This type of smear falls just short of the maximum change which can be obtained with ovarian follicular hormone. It corresponds to an intermediate type between an early and an advanced follicular stage.

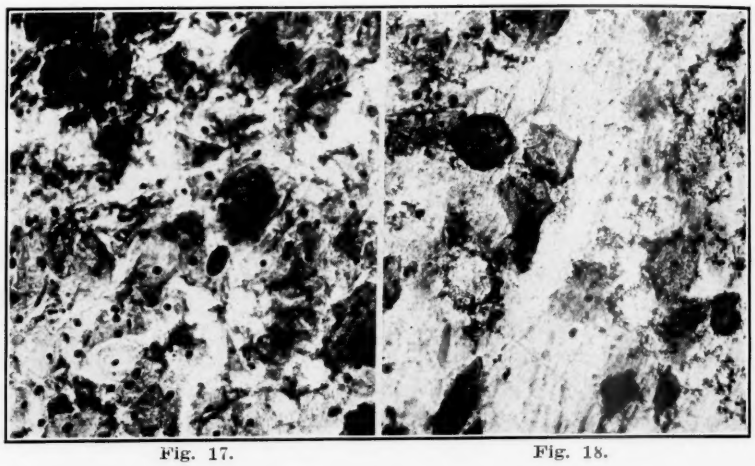

Fig. 17. Fig. 18.

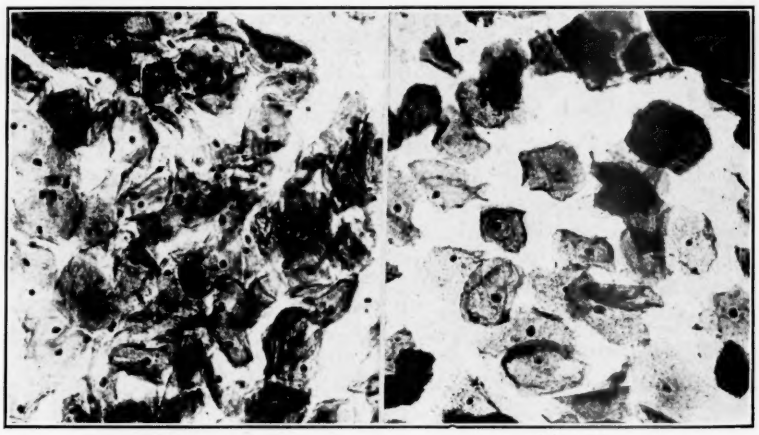

Fig. 19. Fig. 20.

PLATE V. PHOTOMICROGRAPHS OF HUMAN VAGINAL SMEARS.

Fig. 17.—Case W. G. Original type of menopausal smear before treatment. Note dense grouping and poor outlines of cells. Leucocytes fairly numerous but degenerated. One oval deep cell to be seen.

Fig. 18.—Case W. G. Mucous stage. Early effect of oral treatment. Note abundance of mucus and typical fibrination.

Fig. 19.—Case W. G. Leucopenic grouped stage induced by further oral treatment.

Fig. 20.—Case W. G. Early follicular phase induced by further oral treatment. Note leucopenia and appearance of flat enlarged cells with pyknotic nuclei.

The complete relief of symptoms occurred on June 19, some days before the final smear change was achieved. It is of interest that during the period when the smears were stationary at the stage shown in the preceding figure (19), clinical improvement was progressive, although some of the symptoms persisted in mild form.

Treatment was reduced to 2,000 R.U. orally on June 22 and 23 and then stopped entirely. On the evening of June 23 a number of erythrocytes were observed, the smear still remaining at the follicular phase. A typical regression of the vaginal smear then took place. Symptomatic relief continued up to July 17, twenty-four days after the cessation of therapy, at which time mild headaches and numbness of the extremities reappeared. By July 24, moderate flushes had recurred with increased nervousness and some depression.

It is evident that the oral administration of the ovarian follicular hormone may induce comparable changes in the vaginal secretion and symptomatic relief as after hypodermic administration. At this stage, we are not prepared to make a definite statement as to the relative efficiency of the two methods of administration. This point is under study in a group of carefully calibrated cases. Results up to the present indicate that a minimum of 15-20 times the hypodermic dose must be administered orally to produce comparable effects.

The two cases, described above, have been selected as examples of the reactions obtained in our series of well over 50 menopausal cases. The results with this series of cases show a great variability with respect to the dose necessary to induce morphologic and symptomatic changes. Our experience has been that, with adequate doses, which occasionally may be very high, the greater resistance to treatment manifested by some patients, can be overcome.

DISCUSSION

The method of study of the sexual cycle in animals by means of the vaginal smear was introduced by Stockard and Papanicolaou in 1917.[14] Applying this method to ovariectomized mice, Allen and Doisy in 1923[2] developed an exact procedure for demonstrating the action of the ovarian follicular hormone. In 1927, Allen[1] extended the work to ovariectomized monkeys and was able to induce an hypertrophy of the vaginal epithelium, and a modification of the vaginal secretion from the castrate to the normal interval type with administration of this hormone. Other organs, such as the uterus and mammary glands, also responded to treatment. After injections were discontinued, "typical but scanty menstrual bleeding in 7 out of 10 animals" was observed. Davis and Hartman in 1935[3] confirmed the action of the hormone on the vaginal epithelium of the ovariectomized monkey.

The effect of the ovarian hormone has subsequently been demonstrated in human beings. In 1929, Dierks[4] was able to induce an hypertrophy of the vaginal epithelium in a young woman whose

ovaries had been removed. Kaufmann,[7] Werner and Collier,[15] and others have shown that endometrial hyperplasia follows the use of the hormone in menopausal conditions.

We have employed the vaginal smear method in the study of the effects of the ovarian follicular hormone in women because of its simplicity, as well as its other advantages. It permits of daily observations without inconvenience or trauma to the patient. It is also very sensitive and enables one to observe minor reactions as well as advanced changes. Microscopic bleeding can be readily detected.

The validity of this method of study depends on the existence of a close correlation between changes in the vaginal secretions and those taking place in the various organs of the genital tract. Such a correlation was originally demonstrated in the guinea pig[14] and has subsequently been found in other mammals. Of particular interest are the experiments of Allen[1] cited above, showing such a correlation in the monkey since they were carried out under experimental conditions similar to those of the present study.

The relation between the vaginal secretion and the vaginal epithelium in women has been studied by us in a series of biopsies in association with various smear types, during the normal cycle as well as in the menopause. A correlation between the composition of the smear and the structure of the vaginal epithelium was invariably noted.[12]

While considerable experience is necessary to evaluate the morphologic changes in the vaginal secretion which occur in the normal menstrual cycle and in menstrual disturbances, the alterations which we have described in this study are uniform and should be easily recognized by those trained in microscopic work.

THE SIGNIFICANCE OF THE SMEAR CHANGES INDUCED BY THE OVARIAN FOLLICULAR HORMONE

The changes in the vaginal smear and epithelium in the menopausal or ovariectomized state, with administration of the ovarian follicular hormone, are comparable to the alterations which occur during the midmenstrual phase of the normal menstrual cycle when the follicles are reaching their maximal development prior to ovulation.

These changes resemble, even more closely, the periodic appearance of the follicular phase in the postmenopausal state.[10] We had the opportunity to observe such spontaneous alterations in several women with typical symptoms of the menopause. In one such case, during the period of observation prior to treatment, the menopausal smear was gradually replaced by a follicular type of smear, which lasted for about twelve days. A short period of bleeding followed and then the

smear slowly returned to its original type. The menopausal symptoms which had been severe disappeared during the twelve days in which the follicular phase persisted, and gradually reappeared during the regression. The same phenomenon occurred twice within six months in this patient, the second time reinforcing an inadequate dose of hormone.

Spontaneous periodic improvement in symptoms of a temporary nature is not uncommon in the menopause. An explanation for this hitherto obscure phenomenon may be offered by the above observations.

Adequate treatment with the follicular hormone duplicates very accurately these spontaneous changes, both in smear and symptomatology. The progressive improvement in the smear is accompanied by subjective relief which reaches its maximum when the follicular phase is achieved. Likewise with cessation of treatment a short period of bleeding ensues, and then a slow return to the original smear type, during which there is a gradual reappearance of symptoms.

The complete analogy between the spontaneous and experimental changes offers the key to a better understanding of the menopausal state, and furnishes a new therapeutic goal. This is the induction and maintenance of the follicular phase with its associated symptomatic improvement by adequate amounts of hormone.

One should bear in mind that the menopausal type of smear is invariably present after menopause, whether or not symptoms exist. In the latter instance it acquires special significance in that it furnishes an objective index of the symptomatic state. The morphologic changes in the smear, during treatment are accompanied by subjective improvement. The correspondence between the extent of the smear change and the degree of relief is, however, relative, so that it cannot be stated that any particular phase in the changing smear is related to a definite intensity of symptoms. In many patients under treatment a good agreement exists between subjective improvement and the extent of smear change. In others, marked symptomatic relief may precede the attainment of the final follicular phase. In all cases, however, the optimum smear change is accompanied by maximum relief.

On cessation of treatment, the tempo of the regressive changes in the smear, and the reappearance of symptoms is variable. As a rule, the alterations in the smear are gradual, and usually precede the reappearance of severe symptoms. Subsequently a new equilibrium between smear and symptoms is reached. This may be at the original or at a somewhat higher level. In the latter instance, which is the more common, the symptoms persist in a milder form, and the smears fail to show complete regression over a long period.

The prolonged administration of adequate amounts of hormone tends to perpetuate the follicular smear type rather than to produce

further changes in its morphology. It is on the withdrawal or the diminution in the amount of hormone that further alterations in the smear or vaginal epithelium set in. These are in the form of regressive changes which may be accompanied by a brief period of bleeding, as described above (Fig. 16).

Similar regressive changes accompanied by bleeding often appear at the end of the follicular phase in the postmenopausal cycle. During the normal sex cycle corresponding changes appear after ovulation, which may result in a brief postovulatory bleeding. On this basis, one may be justified in considering the withdrawal bleeding as analogous to postovulatory, rather than to true menstrual bleeding. The type of smear during this bleeding which has been described above is in favor of this view.

The above interpretation differs from the current opinion which regards withdrawal bleeding as homologous to menstruation.[1] The latter view has led to the assumption that menstruation is the direct result of the disappearance or diminution of the ovarian follicular hormone.

When large amounts of hormone are administered over long periods, bleeding may occasionally appear during treatment. This bleeding is probably a result of the pronounced uterine hyperplasia and congestion which occur under these conditions. It is evidently of a different nature from withdrawal bleeding. Other workers[15] have also observed this type of bleeding.

A third type of bleeding, which has been largely overlooked up to now, is that associated with the menopausal type of smear prior to treatment. It is generally scant and unnoticed by the patient. It is characterized by the presence of varying numbers of erythrocytes which are almost constantly seen in the smears. There is a pronounced leucocytosis. Deep cells are almost invariably present and usually abundant. Such bleeding may occasionally increase in intensity and become overt.

It is to be emphasized that this type of bleeding rapidly disappears under treatment with ovarian follicular hormone. From this it is apparent that this hormone possesses definite antihemorrhagic properties under certain conditions which need a further analysis and study.

The ready response of this atrophic type of bleeding to treatment with ovarian follicular hormone suggests that it is on the basis of an ovarian insufficiency associated with the menopause. Its proper diagnosis would undoubtedly help to obviate treatment with more drastic measures.

The above considerations make it clear that great caution must be exercised in the interpretation of various types of bleeding. Their

association with definite types of vaginal smears permits in certain respects a more accurate means of differentiation and classification.

The interruption of intensive treatment at intervals of four to six weeks is, in our opinion, highly desirable. These interruptions prevent the uterine hyperplasia from becoming excessive by permitting periodic regressions of the endometrium. In this way, the cyclic changes taking place during normal menstrual activity are simulated. If treatment with large doses is continued for longer periods, women with intact uteri are likely to have profuse and debilitating withdrawal bleeding. Treatment may again be resumed when the recurrence of symptoms warrants it.

The question of the possible relation between estrogenic substances and the development of tumors has been repeatedly raised. In our series, which has been under rather intensive treatment for some three years, there has been no evidence of the appearance of newgrowths. It must, however, be emphasized that this period is too short to permit of definite conclusions.

CLASSIFICATION OF SMEAR TYPES

A classification of the progressive stages in the transition of the menopausal smear to the follicular type would greatly assist in the uniform evaluation of the effects of treatment. A detailed description of the morphologic changes would be too extensive for the scope of this paper and too cumbersome for practical use. Furthermore the variability in the initial smear picture and the overlapping in some of the alterations under treatment would render a rigid schema inaccurate and misleading. A simple system can, however, be suggested into which the most fundamental changes in the significant elements of the smear may be fitted.

This has been done in Table II. The alterations in the constituents of the smear have been arranged, as far as possible, in the order in which they usually appear, and in relation to each other. It should be remembered that there is much overlapping, and considerable variability in the tempo of the various changes. Leucocytes and deep cells, for example, may disappear unusually early, or persist in small numbers at relatively advanced stages. The descriptive terms,—early, moderate, advanced, and complete,—are considered preferable to the designation of stages by numbers.

One of the chief obstacles to a rigid classification appears to be the variability in the original menopausal smears. As has been pointed out, this arises from the differences in the degree of atrophy of the genital organs and the cyclical changes which persist after menopause. Although the character of the original smear bears no relation to the intensity of symptoms in patients with the menopausal syndrome, it

TABLE II. CLASSIFICATION OF MENOPAUSAL SMEAR TYPES AND TRANSITIONAL STAGES DURING TREATMENT WITH OVARIAN FOLLICULAR HORMONE

SMEAR ELEMENTS	MENOPAUSAL SMEAR BEFORE TREATMENT		EFFECT OF TREATMENT ON SMEAR			
	TYPICAL ATROPHIC	VARIATIONS	EARLY	MODERATE	ADVANCED	COMPLETE
Mucus	Moderate or scant. Rarely abundant	Same	Abundant	Moderate or scant	Moderate or scant	Moderate or scant
Leucocytes	Numerous	Numerous or moderate. Rarely leucopenia	Diminishing	Progressive diminution	Relative leucopenia	Leucopenia
Erythrocytes	Usually present in moderate numbers. Rarely numerous. Often fibrination	Less frequent; in small or moderate numbers	Unchanged or increased in number. Fibrination	Diminished or absent	Absent	Absent
Clearness of smear	Hazy or "dirty." Rich in bacteria	Same	Usually unchanged	Progressive clearing	Clearer	Clear
Deep cells	Numerous	Less numerous. May be rare or absent	Unchanged or decreased in number	Diminished or absent	Absent or very rare	Absent
Superficial cells	In varying numbers	Numerous; prevailing	Usually unchanged. Cells less numerous in general	Sharper outlines. Elongate or navicular forms often numerous	Sharper outlines. Flatter. Cells with small nuclei increase in number	Sharp outlines. Larger. Flatter. Cells with small pyknotic nuclei prevailing
	Irregular or folded. Poorly outlined; most with large nuclei	Same type. Cells with small nuclei less frequent; rarely prevailing				
Grouping of cells	Moderate	More pronounced. Often dense smudgy clumps	Very little or no change	Progressive spreading. Sometimes dense groups persist	More spreading; more isolated cells	Smaller, looser groups; many isolated cells
Typical cornified cells	Absent	Absent	Absent	Usually absent. May begin to appear	In varying numbers	Many

will modify, to some extent, the changes taking place under treatment. For this reason it may be of value to describe the several types which have appeared with sufficient frequency and uniformity as to be readily recognized.

a. *The Menopausal Atrophic Type.*—This is most frequently seen in the surgical menopause. It is apparently dependent on absent or minimal ovarian activity, and is associated with an advanced atrophy of the genital tract. It is characterized by an abundance of well-preserved leucocytes and deep cells, and varying numbers of erythrocytes. Mucus is moderate in amount and bacteria profuse. From this starting point (Fig. 2), the whole sequence of changes to the follicular type, as described above (Case E. G.), will usually take place.

b. *The Intermediate Type.*—This is marked by a prevalence of superficial cells in relation to the deep cells, which are also present in fairly large numbers. The superficial cells are irregularly formed, folded, and densely grouped. They have relatively large nuclei. The leucocytes are usually numerous, but poorly preserved. Erythrocytes may be present or absent. Mucous is moderate and bacteria abundant.

c. *The Mucous Type.*—This is featured by an excess of mucus, usually associated with some bleeding and typical fibrination. Deep cells may prevail or be less numerous than the superficial cells. Leucocytes are abundant, but diluted by the profuse mucus, as are the bacteria which are also present in large numbers.

d. *The Premenstrual Type.*—This has a strong resemblance to the normal premenstrual smear.[9] The cells are irregularly folded, appear in dense clumps and have relatively large nuclei. The leucocytes are usually numerous but poorly preserved. Erythrocytes may be present or absent. Mucus is, as a rule, moderate in amount, but may be scant or relatively abundant. The bacterial flora is rich. Deep cells are usually absent, and, when present, are rare.

e. *The Bacillus Vaginalis Type.*—This is characterized by a rich growth of a bacillus closely resembling the Döderlein bacillus. Superficial cells with relatively large nuclei prevail. Deep cells may be present in moderate numbers or absent. One of the chief features of this smear type is the fragmentation of the cells and the liberation of large numbers of nuclei. Leucocytes are present in fair numbers, but mostly degenerated and fragmented. Erythrocytes may or may not be present. Mucus is usually moderate.

f. *The Pseudo-leucopenic Type.*—This is marked by a pronounced leucopenia. Leucocytes may be found, but are usually degenerated or fragmented. Most of the cells are of the superficial type, irregular, and heavily grouped. The nuclei, as a rule, are relatively large, though small nuclei may prevail in some cases.

A smear with a prevalence of small-nucleated cells and with a relative leucopenia may be misinterpreted as indicating a strong follicular reaction. There is, however, a great difference between a smear of this type and a typical follicular leucopenic smear. In the latter the cells are larger, flat, and much more loosely grouped, and many are cornified.

The presence of leucopenia or of an excess of leucocytes in human vaginal smears may occasionally offer some difficulty in interpretation. Certain extraneous factors, such as sexual intercourse, may temporarily increase the number of leucocytes, or the amount of mucus. In evaluating smears one should consider such factors, and lay special stress on the morphologic changes affecting the epithelial cells.

It is of particular significance that all the vaginal smear types described above may be found in cases of amenorrhea. The *menopausal atrophic* type is characteristic of cases of primary amenorrhea, being associated with an infantile uterus. The deep cells prevail in this type. In secondary amenorrheas, all the other types described above are found. The *premenstrual* and the *Bacillus vaginalis* types are the most common. The *Bacillus vaginalis* smear is also common in sterility. In the menopause it has been repeatedly found in association with severe psychoneurotic symptoms. The *pseudoleucopenic* type is relatively rare in the amenorrheas as well as in menopause.

A further similarity between the vaginal smears in the amenorrheas and menopause is that they react in the same way to treatment with ovarian follicular hormone, going through the same transitional stages and reaching the same final (follicular) phase.

The resemblance of the smears in these two conditions, the similarity in their response to the follicular hormone, and the existence of postmenopausal cyclic changes, tend to break down the sharp distinctions generally held to exist between them. From the morphologic standpoint it is frequently hard to classify cases in one group or the other.

CLINICAL CONSIDERATIONS

The question arises whether, apart from the theoretical interest of these observations, the method of the vaginal smears, as outlined above, can be usefully employed. At the start of this work, three years ago, the preparations available were of low potency, and many failures were reported. Considerable pessimism regarding therapeutic possibilities was expressed. With the vaginal smear as a guide, we were led to use increasingly larger doses and came to recognize that the fault lay not in the inefficacy of the hormone but in the inadequate doses customarily employed. The reasons for therapeutic failures in certain patients receiving relatively large doses, such as 1,000 to 2,000 R.U. daily, became apparent when satisfactory changes failed to appear in the smear. Great differences in the maintenance doses in individual patients were found. Such cases could not have been properly interpreted without the information offered by the vaginal smear.

Other considerations support the use of the smear. When subjective symptoms alone are relied on, the physician may be inclined to depend on the more common ones such as the flushes or headache to mark the upper limit of dosage, and regard the many associated complaints as not being of menopausal origin. In this way, much of the benefit inherent in this treatment will often be lost, since the hot flushes frequently respond to the treatment sooner than any other symptom. Smears also permit one to distinguish symptoms of nonmenopausal origin, for which other causes should be sought, for these

will persist after complete smear changes are obtained. This has been of special assistance in the psychic disturbances associated with the menopause which have come to our attention.

In this type of patient, in whom the problem is largely psychiatric, and the usual menopausal symptoms absent or not prominent, the induction and maintenance of the follicular phase offers a reliable method of testing the possible beneficial effects of such treatment. Such a group is now under study. It is of interest that we have repeatedly found severely psychoneurotic patients highly resistant to treatment both as regards smear changes and symptomatic relief. This phenomenon may throw light on the relationship of the menopausal syndrome to psychic states.

There is usually a good correlation between the degree of smear change and the extent of the relief of symptoms, particularly in the severe cases. In many cases, symptomatic improvement precedes the final changes in the smear. Even with the initial mucous phase, which is often induced by relatively small doses, some amelioration of symptoms may be reported. It is this type of relief that may have been experienced by patients who have been reported as responding to small doses. After cessation of treatment relief is maintained for a variable time during which the smear regresses. In some patients this may be a month or more, in others only a few days.

The fact that symptomatic relief may occur before the final smear change, raises the question whether the optimum state is reached when symptoms are relieved or when the follicular phase is induced. Analogies are numerous with other deficiency states, in which objective as well as subjective criteria are available. The relief of the symptoms of myxedema at lower than normal basal metabolic levels, and the abolition of tetany, with the blood calcium and phosphorus still far from normal, are examples. Such partial changes are welcome from the standpoint of the patients' comfort. But it is generally recognized that they are less desirable than the complete restoration of the physiologic state prevailing with the normal function of the hormones involved. It is for this reason as well as the other considerations mentioned above, that we are inclined to consider the induction of the follicular phase, as the more reliable standard in the treatment of the menopause syndrome.

The following general procedure may be adopted in the application of the vaginal smear method to the treatment of the menopausal syndrome. A gynecologic examination should be made to rule out organic disease or the presence of local disease, such as erosions of the cervix or vaginitis, which may affect the vaginal secretion. A small number of control smears should be taken. Treatment can then be started with minimum doses of 250 to 500 R.U. daily for approxi-

mately a week and then a slide examined. The extent of the smear change will direct subsequent treatment. Weekly examination of the smear should be made with progressive increases in dosage until a satisfactory smear change and relief of symptoms are achieved. This procedure can be varied by giving large doses at wider intervals preferably not longer than three days apart. In this case much larger doses will be needed.

The usual effective dose lies between 500 and 2,000 rat units daily, the most common being 1,000 to 2,000 R.U. A few cases respond to 250 R.U., while more resistant ones may need as high as 3,000 or 4,000 R.U. Daily treatment offers advantages with respect to hormone requirements and steady symptomatic relief, particularly in severe cases. Oral administration may be employed and may have advantages as far as convenience and the maintenance of an even concentration of the hormone. Our experience with the two preparations we have used indicates that much larger amounts, a minimum of fifteen or twenty times the quantity injected, will be required orally for corresponding effects. When the desired state is reached, adjustments in dosage can be tried from time to time, as well as temporary withdrawal of treatment, to evaluate the extent of spontaneous readjustment in each patient.

SUMMARY AND CONCLUSIONS

1. The use of vaginal smears as a method of evaluating the action of ovarian follicular hormone preparations on women with menopausal symptoms resulting from either natural or surgical menopause, is described.

2. Two ovarian follicular hormone preparations were used: Amniotin (keto-hydroxy-estrin) and progynon-B (dihydroxy-estrin). Subcutaneous as well as oral treatment was given.

3. With adequate amounts of these hormones, there occurs a transformation of the vaginal smear from the menopausal, to a leucopenic type, with large flat cells, largely cornified, with small pyknotic nuclei. This is the type of smear which is found normally during the high follicular phase of the menstrual cycle just prior to ovulation.

4. This change in the smear is generally associated with relief of the menopausal symptoms.

5. With cessation of treatment or diminution of dosage, the smears gradually regressed and symptoms reappeared. A short period of bleeding usually followed, which is regarded as analogous to post-ovulatory bleeding.

6. Biopsies of the vaginal wall at various stages during treatment showed a close correlation between the changes in the vaginal epi-

thelium and in the vaginal fluid. As a result of treatment, the vaginal epithelium becomes hypertrophic with the more superficial cells showing cornification and small pyknotic nuclei. The outer basal zone was better differentiated and showed nuclear enlargement and mitoses.

7. The daily dose required to induce complete changes in the smear and disappearance of symptoms varied from 250 to 3,000 rat units. Oral administration required a minimum of fifteen to twenty times the hypodermic dose.

8. The vaginal smear test furnishes a simple objective guide for the treatment of the menopausal syndrome with ovarian follicular hormone.

We wish to acknowledge our indebtedness to Miss Charlotte Street of the Department of Anatomy, and to Miss Margaret Rouchleau of the Endocrine Clinic, for their valuable assistance in carrying out this study.

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Hendriksen, Earle: Primary Endometriosis of the Urinary Bladder, J. A. M. A. **104:** 1410, 1935.

Cases of vesical endometriosis are considered primary when there is no evident contiguity to uterus, tubes and ovaries and there was no preceding surgical trauma to bladder wall or its peritoneal reflection. To 20 cases of this kind, collected from literature, the author adds one new one. A nulliparous woman of twenty-seven years, operated upon previously for appendicitis and again for bilateral pus tubes, complained of increasing diurnal and nocturnal frequency, dysuria and dull aching in left lower quadrant. Repeated urinalyses always were negative. A small mass palpated anteriorly to fundus was taken to be a small subserous fibroid responsible for the symptoms. On the basis of this diagnosis, with increasing discomfort, abdominal operation was done. The palpated mass was found to lie within the bladder wall, and with its removal, bladder cavity was opened. Mass excised together with margin of healthy bladder tissue proved to be an endometrioma. Postoperative course smooth. Vesical endometriosis as a rule exhibits three symptoms: urinary frequency, dysuria and a hematuria, usually starting a few days before menstruation, absent during menstrual interval. Cystoscopy always clinches the diagnosis but had not been done in this case on account of both erroneous palpatory diagnosis and absence of hematuria.

Complete excision of the endometrioma is the method of choice for young women, castration is done in patients near the menopause or if the tumor is too extensive for excision.

GROVER LIESE.

THE MILD TOXEMIAS OF LATE PREGNANCY*

Their Relation to Cardiovascular and Renal Disease

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A SATISFACTORY classification of the toxemias of pregnancy will be the result of combined study by the obstetrician, the internist and the pathologist. Thus far the obstetrician has given us numerous reports of the acute phases of the disorder, a few supplemented by follow-up studies, none very prolonged. The resulting classifications of obstetric origin are based, therefore, upon the clinical observation of the presenting syndrome and take little or no account of the later phases of the malady as revealed in the follow-up.

Internists have made few contributions to the subject, largely through lack of opportunity.

In 1927 Corwin and Herrick,[1] on the basis of clinical study with follow-up, suggested that certain of the toxemias were not independent conditions but were related to other well-known clinical syndromes, particularly nephritis and hypertensive cardiovascular disease. Herrick and Tillman,[2] in 1934 and 1935, carried this study a step further, following 594 cases for an average of 5.6 years. This study was supplemented by eleven necropsies. From the clinical and pathologic data thus gathered it was concluded that two types of toxemia exist: (1) a small group characterized clinically and pathologically as nephritis; (2) a much larger group having the features of cardiovascular disease with hypertension.

In a similar study published in 1935 McKelvey and MacMahon[3] reach like conclusions although they use different terms, a circumstance which brings out the awkwardness of present obstetrical nomenclature. These authors state that they use the term "chronic nephritis in the sense employed by Stander and Peckham (1926)" but imply that the condition described is the general vascular disease called, by MacMahon and others, malignant hypertension, and not chronic nephritis. It is true that Volhard and Fahr, and Fahr, have used the term malignant nephrosclerosis to describe this lesion, but this term is unfortunate because it fixes attention upon the kidney while the lesion is one general throughout the entire arterial tree. To confuse this disease with nephritis is to be blind to a well and long accepted opinion of the medical clinic and of the pathologic laboratory.

Bell[4] believed that he had uncovered a peculiar form of kidney disease in a patient who died seven years after an eclamptic pregnancy. Careful reading of this account leads to the conclusion that the case was an example of cardiovascular disease with hypertension. Bell himself suggested that "the capillary thickening and hyalinization of the glomeruli were evidence of a peculiar disease of the kidney" but that the "findings, including cardiac hypertrophy, suggest that the

*Read at a meeting of the New York Obstetrical Society, December 10, 1935.

patient must have had hypertension.'' Löhlein,[5] in 1918, compared the swelling and increase of the capillary epithelium and thickening of the capillary walls in eclampsia with the picture of glomerulonephritis although he distinctly did not identify them as the same lesion. Baird and Dunn[6] found the glomeruli in eclampsia ''notably bloodless,'' noted that ''leucocytes were conspicuously few,'' commented that in 9 of 10 cases of eclampsia the ''constant and predominant lesions were found to be in the glomeruli and to correspond closely with those described by Löhlein, Fahr and Bell,'' and concluded that the ''common lesion in the kidneys in fatal eclampsia is glomerular and is characterized by thickening of the capillary walls and of endothelium leading to some degree of obstruction to blood flow.''

At this point one might call attention to the association of artificially induced renal ischemia and arterial hypertension as shown experimentally by the recent work of Goldblatt, et al.[7] and its confirmation by Page.[8] The possible application of these findings to the mechanism of hypertension in certain pregnancy toxemias is at least suggestive.

Heynemann[9] collected 7 cases which came to necropsy from two to twenty-four years after an eclamptic pregnancy. One of these had been reported by Schultz[10] in 1933 with the comment that the patient succumbed to uremia seven years after eclampsia in pregnancy, but that the clinical diagnosis of chronic glomerulonephritis was not borne out by necropsy. In fact, he found no evidence of inflammatory lesions in the kidneys. The pathologic diagnosis was nephrosclerosis. Six of the 7 cases tabulated by Heynemann were diagnosed pathologically as nephrosclerosis, malignant in 3. In 4 the final illness was an apoplexy. The seventh died of a pyelonephritis. Heynemann states, ''In the development of malignant sclerosis and its transition stages eclampsia plays a not unimportant rôle.... If in the follow-up of women who have experienced an eclamptic pregnancy at an earlier time hypertension and albuminuria are disclosed this does not point to the presence of a chronic nephritis but to a nephrosclerosis... The majority of these patients succumb to apoplexy in the end.'' In the 594 cases followed by Herrick and Tillman[2] 80 per cent of the determinable deaths were from causes within the cardiovascular renal field.

Cushing's findings of an invasion of the pars posterior of the pituitary in both essential hypertension and eclampsia, while speculative and not yet accepted in all quarters, may be mentioned as of interest in forming another and different link in the growing chain of evidence joining these two conditions.

As internists with a peculiarly favorable opportunity for the study of all phases of this problem including the symptoms during pregnancy, those appearing in the follow-up and the findings at necropsy, we record our experience with the group of milder toxemias which have been classified variously as nephritis, albuminuria of pregnancy, recurrent toxemia, and low reserve kidney. In discussing this group Stander states that it is a mild toxemia of the latter half of gestation and that if the patient's ''blood pressure is normal until about the middle of pregnancy and then begins to rise, it is undoubtedly due to a toxemic condition directly associated with the pregnancy and is not essential hypertension.'' The criteria for this type may be quoted from Stander.[11]

1. An elevated blood pressure which at the end of the puerperium has dropped to a normal level. In most instances this elevation is not marked, rarely exceeding 150 systolic and 90 diastolic.

2. The amount of albumin in the urine is never very great, varying before delivery between a fraction of a gram and 2 grams per liter, although the lower figures are most usually observed. The albumin disappears during the puerperium and the patient leaves the service either with no albumin at all, or with at the most 0.1 gram per liter.

3. The outstanding characteristic is the fact that in subsequent pregnancies the patient's condition does not become aggravated, and she is as well as, or better than, she was in the preceding pregnancy. Each of our 14 cases clearly demonstrates this point.

4. The blood chemistry as well as the urinary analysis reveals nothing abnormal.

That the number of pregnancies through which the individual may go plays any rôle in the development of this entity is very doubtful for the reason that we observe it in primiparas as well as in all degrees of multiparity. . . . All we can say is that the kidney reserve seems to be too low to meet the extra demands of pregnancy as is manifested by the passage of a certain amount of albumin through the glomerular epithelium and by a moderate elevation of blood pressure, and that these manifestations usually disappear completely within two weeks after delivery. Furthermore, the kidney substance does not seem to have been injured by pregnancy and the kidney reserve is certainly not lower in subsequent pregnancies.

By leaving out of consideration all other groups, and by conforming strictly to this definition we have been able to select 188 cases for special study. No case followed for less than one full year was included. The period of follow-up ranged from one to twenty-four years, the average being seven years. All cases complicated by rheumatic heart disease, thyroid disease or any other disorder which might influence the blood pressure were excluded. Conforming to the definition quoted, none showed elevation of the systolic blood pressure of more than 150 mm. Hg

TABLE I

HIGHEST ANTEPARTUM BLOOD PRESSURE: SYSTOLIC	CASES	FOLLOW-UP BLOOD PRESSURE: SYSTOLIC				
		UNDER 130	130-139	140-149	150-159	160 plus
130-139	11	5		5		1
140-149	89	29	14	17	13	16
150	88	14	19	18	13	24
Total	188	48	33	40	26	41

TABLE II. GROUP OF 63 CASES WITH HYPERTENSION IN THE FOLLOW-UP

SYSTOLIC BLOOD PRESSURE	130-139	140-149	150-159	160-179	180-199	200 plus	Total
Cases	2 (High diastolic)	8 (High diastolic)	10	27	11	5	63
DIASTOLIC BLOOD PRESSURE	to 90	90-99	100-109	110-119	120-129	130 plus	Total
Cases	2 (High systolic)	13	28	10	8	2	63

and of the diastolic above 90 mm. Hg excepting an occasional case with a transitory rise of either the systolic or of the diastolic blood pressure to 160 or 100 to 110 mm. Hg, respectively. None was included in which such exaggerated elevation of both systolic and diastolic pressure was simultaneous or occurred in the same individual. None showed more than a trace of albumin at any time in the antepartum period, and some showed none at all. Edema was seldom present, convulsions did not oc-

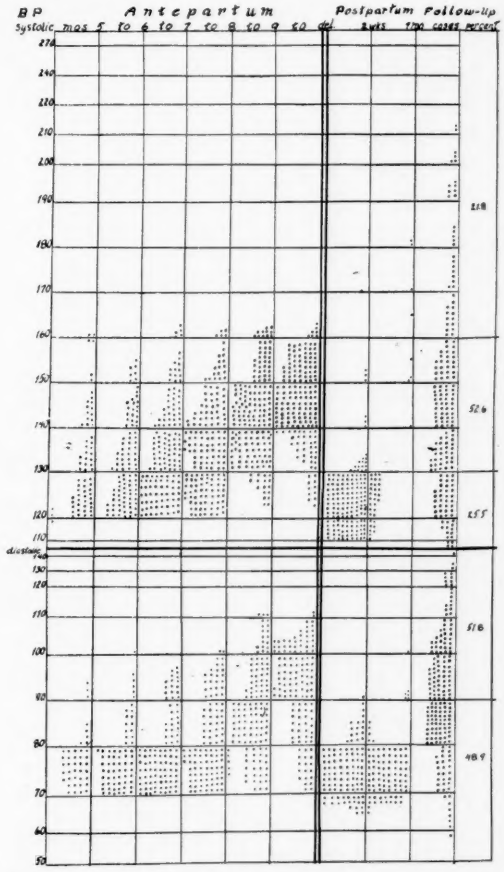


Chart 1.—Blood pressure readings in 188 cases, antepartum, during the puerperium, and at the last follow-up observation.

cur and reflex hyperexcitability or other signs of implication of the nervous system were absent. In the postpartum period practically all showed a fall of the blood pressure to normal. A comparison of the antepartum and follow-up blood pressure (systolic) is illustrated in Table I.

It is interesting to note that of the 188 cases, 63, or 33.5 per cent, showed hypertension in the follow-up, with a range from 150 to 260 mm. Hg systolic and 90 to 160 mm. Hg diastolic (Table II). It is also interesting to note that in practically all of the cases in this minor group

showing hypertension in the follow-up the blood pressure postpartum was normal (Chart 1). This drop of a hypertension to a normal pressure in the puerperium is very striking. Along with the hypertension the follow-up revealed other stigmas of cardiovascular disease, such as ocular changes, especially in the retinal vessels; cardiac enlargement; obvious thickening of the brachial vessels; vasomotor or circulatory symptoms such as headaches, dyspnea, palpitation. The incidence of these is shown in Table III. Albuminuria was generally absent, or present as a trace only.

TABLE III

SIGNS AND SYMPTOMS IN THE FOLLOW-UP	GROUP OF 63 CASES WITH HYPERTENSION		GROUP OF 125 CASES WITH BLOOD PRESSURE BELOW 150 MM. HG SYSTOLIC	
	CASES	%	CASES	%
Retinal vascular changes	33	52.4	29	23.2
Albuminuria	20	31.7	20	16.0
Cardiac symptoms	20	31.7	18	14.4
Edema, however slight	7	11.1	11	8.8

It has been frequently noted that women with toxemia of pregnancy have a certain bodily habitus. They are likely to be short and stout, inclining to plethora. Table IV shows that in the group with hypertension in the follow-up the average weight was higher than in that with normal blood pressure or only a slight rise in the follow-up.

Similarly, studies in height, illustrated in Table V, emphasize that the majority of women in both groups were of small stature, though no

TABLE IV

WEIGHT IN FOLLOW-UP (POUNDS)	GROUP OF 63 CASES WITH HYPERTENSION		GROUP OF 125 CASES WITH BLOOD PRESSURE BELOW 150 MM. HG SYSTOLIC	
	CASES	%	CASES	%
To 100	1	1.6	1	0.8
100-109	5	7.6	14	11.2
110-139	9	14.8	37	29.6
140-159	10	15.8	36	28.8
160-179	10	15.8	17	13.6
180-199	8	12.7	7	5.6
200 plus	12	19.0	3	2.4
Not noted	8	12.7	10	8.0

TABLE V

HEIGHT	GROUP OF 63 CASES WITH HYPERTENSION		GROUP OF 125 CASES WITH BLOOD PRESSURE BELOW 150 MM. HG SYSTOLIC	
	CASES	%	CASES	%
Under 5′	3	4.7	10	8.0
5′ to 5′ 2″	22	35.0	43	34.4
5′ 3″ to 5′ 5″	28	44.4	48	38.4
5′ 6″ and over	3	4.7	16	12.8
Not noted	7	11.1	8	6.4

TABLE VI

AGE	AGE AT TOXIC PREGNANCY				AGE AT FOLLOW-UP							
					CASES WITH HYPERTENSION IN F. U.				CASES WITH B. P. BELOW 150 MM. HG IN THE FOLLOW-UP			
	MULTIPARAS		UNIPARAS		MULTIPARAS		UNIPARAS		MULTIPARAS		UNIPARAS	
	CASES	%	CASES	%	CASES	%	CASES	%	CASES	%	CASES	%
To 19	1	1.5	3	5.1								
20-24	18	27.1	25	43.1			1	1.7	4	6.0	11	19.0
25-29	24	36.3	13	22.4	2	3.0	6	10.3	11	16.6	17	29.3
30-34	17	25.7	9	15.5	5	7.4			14	21.2	9	15.5
35-39	6	9.0	6	10.3	9	13.6	5	8.5	7	10.6	3	5.1
40-44			2	3.4	3	4.5	2	3.4	2	3.0	2	3.4
45-49					3	4.5	1	1.7	4	6.0	1	1.7
50					1	1.5						
Not yet del.									1	1.5		
Total	66	99.6	58	99.8	23	34.5	15	25.6	43	64.9	43	74.0

striking contrasts are presented. The studies of age incidence show nothing remarkable (Table VI). There seems to be no indication that women in the more advanced age groups are more prone to this mild toxemia of pregnancy.

Since a point has been made of the importance of behavior in subsequent pregnancies as a basis of classification, attention may be given to this group (Table VII). Of the 188 cases, 66 were observed through more than one pregnancy at Sloane Hospital. The fetal mortality was nil. But since not all women showing toxemia of any type necessarily

TABLE VII

TOXEMIA IN SUCCEEDING PREGNANCIES AS JUDGED BY B. P.	SYSTOLIC BLOOD PRESSURE IN THE FOLLOW-UP					
	TO 130	130-139	140-149	150-159	160 PLUS	TOTAL
Increased	3		6	1	14	24
Same	4	4	7	6	2	23
Less	6	1	1	1	1	10
Normal	4	1	3			8
In last pregnancy only					1	1

experience another pregnancy, we also grouped those who were primiparas when they came to us and who have not had another pregnancy. There were 58 primiparas in the 188 cases and their blood pressure in the follow-up is shown in Table VIII. As a matter of interest the

TABLE VIII

UNIPARAS	SYSTOLIC BLOOD PRESSURE IN THE FOLLOW-UP					
	TO 130	130-139	140-149	150-159	160 PLUS	TOTAL
Cases	16	13	7	7	15	58
Per cent	27.6	22.4	12.0	12.0	25.8	100.0

uniparas and multiparas are grouped together in Table IX, from which it becomes clear that so far as her ultimate blood pressure is concerned uniparity will not protect the woman against eventual hypertension, as

TABLE IX

GRAVIDITY	FOLLOW-UP BLOOD PRESSURE: SYSTOLIC										TOTAL
	TO 130		130-139		140-149		150-159		160 PLUS		
	CASES	%	CASES	%	CASES	%	CASES	%	CASES	%	
Uniparas	16	27.6	13	22.4	7	12.0	7	12.0	15	25.8	58
Multiparas	17	25.7	6	9.0	17	25.7	8	12.1	18	27.1	66

compared with the fate of her multiparous sister. It may be remarked that the requirement of basing a classification of a toxemia upon the patient's behavior in later pregnancies (which may never occur) is, to say the least, awkward and unsatisfactory. Perhaps more precise knowledge will show that it is not necessary to invoke such an uncertain factor in assigning to the milder toxemias their proper place among the toxemias.

In the hope of making a contribution, even a negative one, to a clearer conception of the mild toxemias, we have attempted to trace the ultimate fate of such patients and especially to determine the eventual presence or absence of kidney disease or other stigmas in this group of so-called low reserve kidney after prolonged follow-up.

The recognized forms of kidney disease, the nephroses, the nephritides, and those secondary to arteriosclerotic vascular changes, are based upon consistent clinical and pathologic features which need not be reviewed here. There is ample evidence to show that nephritis complicated by pregnancy is a recognizable condition with a quite definite course and prognosis. There is satisfactory evidence that eclampsia and pre-eclampsia in many of their acute manifestations and particularly in their sequelae and end-results are allied to what is variously termed hyperpiesis, essential hypertension or arteriolar nephrosclerosis. In considering the milder toxemias of pregnancy which are neither eclamptic nor nephritic in the strict sense are we dealing with an altogether new set of conditions for which we must invent new terms or can they be fitted into sound established categories?

For purposes of study of this group where theory and vague terminology abound we have selected from our 188 cases of mild toxemia those showing hypertension, not immediately postpartum, but in the follow-up period of from one and one-half to nineteen years. By the selection of those with the most pronounced functional disturbance we believe we can reach the fairest judgment as to the rôle of the kidney in the entire process from its inception in pregnancy to its end-result, including, where possible, the necropsy manifestations. Of the 63 cases comprising this group, 35 whose cooperation could be obtained were brought back for tests of renal function. The results are presented in Table X.

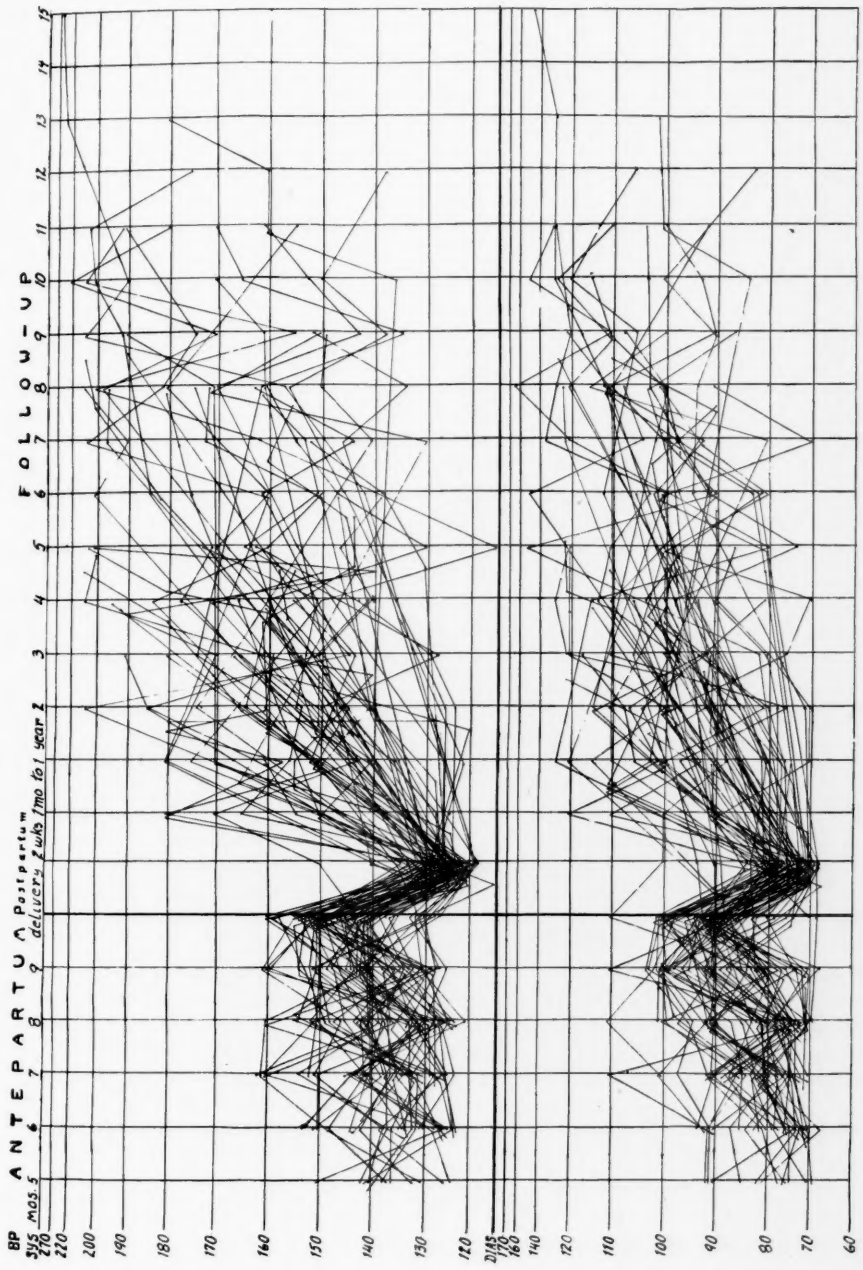
Certain facts emerge from a study of this kind. It would seem clear that the mild late toxemia of pregnancy with hypertension is not free from dangerous possibilities in the future. As shown in this study, about one-third will reveal systolic or diastolic hypertension or both within a year of delivery. The initial fall of blood pressure to normal during the puerperal period should not give one a sense of security. Such a fall may be followed by a significant hypertension within one to five years postpartum (Graph I). Study of this group makes one very hesitant to indict the kidney as the source of the difficulty. In a group as large as this, had an incompetent kidney been at the foundation of the disturbance, conspicuous kidney damage should have manifested itself in some of the 188 cases some time in the course of such a long follow-up period, particularly in those revealing appreciable hypertension over a period of years. Here the absent or slight albuminuria, the absence of casts or of red blood cells in the urine, the lack of anemia

TABLE X

CASE	YR. F. U.	B. P. IN F. U.	URINE			UREA CLEARANCE					BLOOD UREA-N MG./100
			DAY SP. GR.	NIGHT SP. GR.	ALB.	I	%	II	%	AVERAGE	
1	10	190/130	1.017	1.009	VFT	c_s – 28.8	53.4	c_s – 34.4	63.6	58.5*	19.8
2	10	190/124	----	----	----	c_s – 49.0	91.0	c_s – 46.6	86.5	88.7	16.0
3	10½	160/100	1.009	1.008	VVFT	c_s – 39.2	72.5	c_s – 36.5	67.5	70.0*	19.2
4	6	160/100	1.023	1.011	VVFT	c_s – 76.3	141.0	c_s – 75.9	140.0	140.5	10.6
5	4½	160/94	----	----	----	c_s – 38.0	70.9	c_s – 22.4	41.5	56.2*	16.3
6	4	200/124	1.023	1.019	o	c_s – 40.5	75.0	c_s – 44.3	81.5	78.2	12.8
7	9	170/115	1.023	1.025	VVFT	c_s – 46.0	85.0	c_s – 42.5	79.0	82.0	12.6
8	1½	154/100	1.015	1.023	o	c_s – 60.0	111.0	c_s – 44.0	81.5	96.2	11.8
9	4	160/90	1.028	1.021	VVFT	c_s – 57.5	106.0	c_s – 84.3	131.0	118.0	18.3
10	10	180/110	1.023	1.012	VFT	c_s – 41.6	77.0	c_s – 36.4	67.5	72.2*	15.3
11	5	174/84	1.023	1.017	VVFT	c_s – 66.6	123.0	c_s – 73.1	135.0	129.0	17.4
12	4	160/90	1.010	1.010	o	c_m – 32.7	43.5	c_m – 48.1	64.0	53.7*	16.1
13	5	200/116	1.024	1.019	VVFT	c_s – 53.8	99.6	c_m – 89.6	161.0	130.3	12.6
14	10	170/110	1.021	1.019	o	c_s – 70.7	131.0	c_s – 87.0	161.0	146.0	9.8
15	3	190/118	1.021	1.020	o	c_s – 75.6	139.9	c_s – 72.6	127.3	133.6	12.8
16	4	148/108	1.011	1.014	o	c_s – 46.3	85.0	c_s – 36.6	67.6	76.3	12.1
17	6	160/100	1.030	1.013	o	c_s – 34.7	64.2	c_s – 42.0	78.0	71.1*	24.8
18	10	146/100	1.029	1.029	VFT	c_s – 81.8	151.0	c_s – 60.6	112.0	131.5	18.6
19	7	160/90	1.014	1.026	o	c_s – 48.1	89.4	c_s – 41.4	76.8	83.1	15.7
20	6	140/104	1.018	1.013	VVFT	c_s – 35.6	66.0	c_s – 33.5	62.0	64.0*	16.3
21	3	180/102	1.010	1.018	o	c_s – 52.6	97.6	c_s – 48.5	90.0	93.8	12.9
22	8	160/104	1.021	1.027	o	c_s – 50.0	92.5	c_s – 50.0	93.5	93.0	17.3
23	12	180/100	1.022	1.019	VVFT	c_s – 55.1	103.0	c_s – 68.3	126.0	114.5	11.5
24	19	176/104	1.018	1.011	VVFT	c_m – 70.4	94.0	c_s – 41.9	77.5	85.7	19.0
25	6	176/104	1.010	1.010	o	c_s – 44.1	82.0	c_s – 38.3	71.0	76.5	10.2
26	10	150/100	----	----	----	c_s – 78.0	144.0	c_s – 63.6	118.0	131.0	11.4
27	3	170/90	1.028	1.032	o	c_s – 22.9	42.3	c_s – 41.9	77.6	59.9*	20.3
28	6	170/90	1.022	1.024	o	c_s – 60.5	112.0	c_s – 52.6	97.5	104.7	10.4
29	9	162/110	1.024	1.018	o	c_s – 76.2	141.0	c_s – 69.6	129.0	135.0	10.6
30	5	172/108	1.021	1.013	o	c_s – 57.5	106.0	c_s – 56.0	103.5	104.7	12.1
31	7	160/100	1.021	1.019	o	c_s – 81.5	151.0	c_s – 86.0	159.0	155.0	9.8
32	4	160/110	1.018	1.017	o	c_s – 69.0	127.5	c_s – 66.0	122.0	124.7	14.0
33	4	168/94	----	----	----	c_s – 47.2	87.5	c_s – 45.9	85.0	86.2	10.2
34	5	200/120	1.021	1.018	VFT	c_s – 44.6	83.0	c_s – 41.8	77.2	80.1	15.1
35	5	162/96	1.012	1.009	o	c_s – 46.8	86.8	c_s – 46.3	85.5	86.1	13.4

*Indicates lowered clearance.

and of nitrogen retention, the benign course over a lengthy period of follow-up, are strong arguments against significant renal participation at any stage of the malady.



Graph I.—Showing the course of blood pressure in the antepartum, puerperal and follow-up periods in 63 cases. These constitute 33.5 per cent of 188 cases and are selected because of hypertension in the follow-up.

The clinician who disregards the findings of the pathologist hazards much. In terms of the necropsy the end-results of eclampsia and of

true chronic nephritis in pregnancy are well known. They present the features of hypertensive cardiovascular disease and of nephritis, respectively.

Naturally, the end-results of the milder types of toxemia are less well known because the sequels are less severe and life expectancy greater. Among 188 cases of this type studied by us one case has come to necropsy.

History.—The patient was a Negress, para viii, aged forty-two years at death. The first pregnancy, in 1918, was characterized by moderate albuminuria and systolic blood pressure rising to 140 mm. Hg in the antepartum period. Later in the same year there was a miscarriage followed by curettage. In 1919 a living child was delivered by forceps, at home. A miscarriage took place in 1922, and in 1924 she went through a normal pregnancy with blood pressure of 126 mm. Hg systolic and 90 mm. Hg diastolic, with a trace of albumin in the urine. Later in the same year there was a spontaneous miscarriage followed by curettage. In 1926 examination in the follow-up revealed a blood pressure of 156 mm. Hg systolic and 110 mm. Hg diastolic, a faint trace of albumin in the urine and definite retinal arteriosclerosis. In 1928 the patient was again delivered at the Sloane Hospital for Women, having had a normal blood pressure throughout pregnancy and no albumin until just before delivery. In 1929 the blood pressure was 214 mm. Hg systolic and 118 mm. Hg diastolic. Being again pregnant in 1930 with persistent hypertension and a faint trace of albumin in the urine, supravaginal hysterotomy was performed. Two months later the blood pressure was 130 mm. Hg systolic and 80 diastolic. Shortly thereafter the blood pressure was elevated to 240 mm. Hg systolic and 126 mm. Hg diastolic with marked cardiac hypertrophy, sclerosis of the retinal vessels, and an accentuated aortic second sound. Two weakly positive and several negative Wassermann reactions are recorded and antisyphilitic treatment was begun in 1931. One year later (in 1932) the blood pressure was 230 mm. Hg systolic and 150 mm. Hg diastolic. Two years later (in 1933) headaches became severe and blood pressure increased to 265 mm. Hg systolic and 145 mm. Hg diastolic. Vomiting, dyspnea, orthopnea, and disturbed mentality occurred. There were marked vascular changes in the retina, edema, increased retention of nitrogen, evidence of myocardial damage, and a terminal pericarditis. Death took place in February, 1933.

At necropsy the anatomical diagnosis was generalized arteriolosclerosis, arteriolonephrosclerosis, cardiac hypertrophy and dilatation, slight arteriosclerosis of the aorta, fibrosis of the myocardium, acute fibrinous pericarditis, chronic passive congestion of the liver, lungs, and spleen, and fibrous peritoneal adhesions.

The arteriolar lesions were pronounced in the arterioles of the spleen, the portal areas of the liver, the pancreas, the kidneys, and suprarenals. These arteriolar lesions were of the acute necrotizing type and accompanied by moderate secondary atrophy in the involved organs. Certain tubular changes in the kidney, particularly the occurrence of an atypical flattened epithelium containing large amounts of refractile brownish pigment which took a pronounced iron stain, suggested the effect of intensive antisyphilitic treatment. The hypophysis showed a definite proportional increase in the basophilic element similar to changes described in cases of hypertension by Krause.

In its clinical features this case was a typical example of the mild toxemia of pregnancy under discussion. Excepting the possible complication of syphilis, the necropsy findings were characteristic of generalized arteriolosclerosis associated with prolonged hypertension.

A single case proves little, but when it fits the picture formed by the clinical aspects of the large series it lends vigor to the argument. When one assembles the findings of a number of observers[1-4, 9, 10] it is clear that the end-result of eclampsia and of preeclampsia is likely to be hypertensive cardiovascular disease with a terminal arteriolosclerosis. So far as it goes the limited evidence here presented points to a like conclusion in examples of the milder types of toxemia.

As one reviews these studies one finds it almost impossible to reconcile the commonly accepted obstetric classification of the toxemias of pregnancy with the findings in the medical follow-up and with the necropsy results. From the clinical and pathologic observations cited, it is possible to place the eclampsias and preeclampsias in a tentative category based upon clinical and postmortem studies after follow-up. The same can be said for the true nephritides. This being granted, there remains a large group of the mild late toxemias which forms a twilight zone in which classification is vague and terminology confusing. By some these have been called nephritis, by others recurrent toxemia or low reserve kidney. In obstetric quarters there is a persistent inclination to indict the kidney as being fundamentally or solely concerned in the disturbance.

From the welter of theory and uncertainty heretofore surrounding the matter of classification of the toxemias of pregnancy ideas soundly based upon clinical and necropsy study begin to take form. When these are fully delineated it is our opinion that we shall find nephritis concerned in but a small fraction of the toxemias; that the larger number, including the eclampsias, the preeclampsias, and the variously designated milder types of late toxemia discussed in this paper will be found to have unit characters based upon cardiovascular disease with hypertension, and not upon nephritis. *Their important components are circulatory and not renal.*

If this point of view is correct it is desirable that the obstetrician gain a clear idea of the differences between these two conditions, that he cease to place so much emphasis upon the kidney, and that eventually, when further clinical and pathological studies are in hand he adopt a soundly based classification. When this desired position has been reached we believe with McCann[12] that such meaningless terms as "low reserve kidney" will be abolished. Perhaps we then shall recognize two chief types of late toxemia: one, nephritic (or rather, nephritis complicating pregnancy), based upon an antecedent or coexisting glomerulonephritis; the other, vascular, allied to or identified with hypertensive cardiovascular disease.

CONCLUSIONS

1. A satisfactory classification of the late toxemias of pregnancy will be the result of combined study by the obstetrician, the internist, and the pathologist, including symptoms during pregnancy, those appearing in the remaining years of the woman's life, and the findings at necropsy.

2. Previous studies have defined the status of nephritis in pregnancy, and of eclampsia and preeclampsia in their relation to chronic inflammation of the kidney and to cardiovascular disease with hypertension respectively.

3. The milder types of late toxemia, vaguely called low reserve kidney, recurrent toxemia or nephritis, in their follow-up and necropsy manifestations, seem to resemble eclampsia and preeclampsia in that their frequent results are general vascular disease with hypertension rather than nephritis. The differences between the severe and milder types of nonnephritic late toxemias are of degree, not of kind.

4. The rôle of the kidney in this disturbance is probably incidental and not fundamental. This organ participates because it is such an important part of the circulation. Placing responsibility upon the kidney primarily seems misleading and to indicate a limited and faulty conception of a process having broader implications.

5. Vague terminology such as low reserve kidney, recurrent toxemia, and so on, confuses thought and should be abolished. The part of general vascular disease in late toxemia of pregnancy needs emphasis.

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The history of the gradual development of specialized care for the parturient, and the rise of the physician into the ranks of "man-midwife" is traced from the time of Hippocrates (400 B.C.) to the early nineteenth century.

The midwife arose in remote times from the custom of a woman attending at the delivery of her neighbor. It became a means of livelihood with some and they devoted their entire time to the trade. The care of the parturient thus fell into the hands of woman and it was deemed her work. Too often a poor type of woman was in the field, and progress in obstetrics was greatly retarded.

Men were barred from the birth room by ignorance and modesty on the part of patient and husband. Thus, in 1522 a Dr. Wertt of Hamburg was forced to put on the dress of a woman in order to attend and study a case of labor. When detected, he was punished by being burnt to death. As late as 1658, Dr. Percival Willoughby, when called into consultation on a possible breech presentation by his own daughter attending the case, crept into the chamber upon hands and knees unseen by the patient, only to examine her in haste under cover.

Many interesting instances of similar nature are recorded. The entry of men into this field and the accumulation of a midwifery literature is described.

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IS SUPERFETATION POSSIBLE IN THE HUMAN BEING?*

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SUPERFETATION in the human being may be defined as the implantation of a second fertilized ovum in a uterus already containing a pregnancy of at least one month's duration. The belief in the occurrence of this phenomenon is of ancient origin. According to Radash[1] its possibility was discussed by Hippocrates, Pliny, and Aristotle. For a most complete review one may refer to an article by this author published in 1921. De Lee[2] in 1933 states that superfetation is held possible by American and French authorities but denied by the English and German.

In a survey of the literature bearing on this subject one finds several varieties of cases quoted in its support. These may be classed in the following groups: (a) Abortions in which two or more fetuses are passed with a marked difference in size and appearance; (b) cases of pregnancy which go to term and deliver two or more fetuses with a marked variation in size. In this group are also patients who deliver a term infant and following a one to three months' interval, deliver a second infant also at term; (c) cases occurring in animals.

The first group, made up of women who aborted two fetuses, obviously differing widely in size and development, has always suggested the possibility of superfetation. Tyler-Smith[3] reported a case in 1856 of a woman who aborted a four to five months' fetus and about half an hour later a healthy well-formed four weeks' ovum. J. C. Longmore[4] in 1862 reported the case of a woman who aborted a dead fetus of three to four months. This was followed by a perfect fresh ovum of four weeks. This specimen was presented before the London Obstetrical Society, was reviewed by a committee and accepted as an instance of superfetation because of the perfect condition of the smaller embryo. Gustatter[5] in 1918 reported the simultaneous abortion of a well-formed, fresh four months' fetus and sac together with a two months' ovum. He assumed this to be a case of superfetation although no microscopic examination was carried out. He felt that this phenomenon was more frequent than was commonly believed and that it was a frequent cause of early abortion. A. W. Meyer,[6] in 1919, reviewed four similar cases from the Mall collection and found that in all instances the smaller fetus was macerated and had been dead for some time. Strangely he does not include any microscopic reports on the placentas. He also gave further findings on the case reported by Gustatter[5] and felt that it was of the same type. He concludes that all these cases are twin pregnancies in which one twin dies in utero followed later by a miscarriage of both living and dead fetuses. Radash[1] in 1921 reports another case, that of a woman who aborted a four months' fetus and a second fetus measuring 1.8 cm. (forty days). He gives a very complete review of the literature and concludes that this is an example of superfetation although no microscopic examinations are included in his report. He

*Presented at a meeting of the New York Obstetrical Society, November 12, 1935.

discusses minutely the definition of this condition and does not think that a second coitus is necessary for superfetation to occur, quoting a case reported by Duerrsen and Zweiffel in support of the prolonged existence of sperm in the female genital tract. They found living sperm in an oviduct removed from a woman in which instance it was positively stated that there had been no coitus for four weeks. Recent work by Hammond and Ansell[7] suggests that sperm do not retain fertility after having been in female generative tract over thirty hours. Ingram-Johnson[8] in 1921 reported the abortion of a five months' living fetus together with a six weeks' ovum as an example of superfetation. Again his examination was rather superficial. Cathala and Barbaro[9] in 1925 reported a case of a woman who aborted a well-formed and unmacerated four months' fetus and sac together with a 2 months' ovum. At first they felt that this represented a superfetation but on further study, the placenta of the smaller fetus showed marked fibrosis and necrosis of the villi. Therefore, in spite of the well-preserved appearance of this fetus, they considered the true explanation to be the death of a twin followed later by the abortion of both fetuses. Moench[10] in 1927 reported a patient with a double uterus who prematurely delivered a seven months' fetus who survived, and, three days later, passed a fresh three months' ovum. He considers this an example of superfetation although he never saw the smaller fetus, depending on the word of the midwife who conducted the case. Willis[11] in 1929 describes one more case of the abortion of a four months' fetus and sac together with a nine weeks' ovum. Because of the fresh gross appearance he concludes that superfetation must be the explanation. However, no thorough study was carried out. In almost all of these patients bleeding took place at intervals during the pregnancy. This was interpreted by the earlier observers as menstruation. In all the cases in which thorough study was carried out, the smaller fetus was found to have been dead for some time before the abortion occurred. The most suggestive case is that reported by Longmore,[4] for in this instance the larger fetus was macerated and the smaller appeared fresh. Moreover, this case was accepted by a committee of skeptics. However, no microscopic examination was made of the smaller fetus or placenta. One may conclude that, although this type of case superficially suggests superfetation, the more probable explanation is the abortion of twin pregnancy, one twin having died some time before this event.

A number of instances falling in the second group are found in the older literature in which women gave birth to term infants and subsequently, in each case, from one to four months later, these mothers underwent a second labor and delivered a second child apparently at term. Churchill[12] in 1846 cites a case reported by Bigaud of Strassburg of a woman who delivered a term infant on April 30. On September 17 of the same year she gave birth to a second term infant. This patient came to autopsy when it was found that she had a single uterus. He also cites the case reported by Boivin of a woman who gave birth to a 4-pound child on March 15, 1810. On May 12, 1810, she gave birth to a second infant weighing 3 pounds. Examination revealed a probable double uterus. Alexander Milne[13] in 1871 cites a case reported by Maton of Palermo of a woman who delivered a term infant on Nov. 12, 1807. On Feb. 2, 1808, or eighty-two days later she delivered a second term infant. Leishman also refers to this case, but considers that the first birth represented the premature delivery of a twin, the second twin being carried to term. Leishman[14] in 1873 refers to a case reported by Möbus at Dieburg of a woman who delivered a healthy term infant on Oct. 16, 1833. Thirty-three days later she delivered a second term girl. Playfair[15] in 1876 refers to an interesting series of cases collected by Bonnar from the records of long-established families. In these cases succeeding children were born at intervals as short as four months. These children all survived. Robert and Fancourt Barnes[16] in 1884 cite a case reported by Naegelé of a woman delivered in Düsseldorf on June 22, 1857, of a large term

infant. One-half hour later she delivered a second child, a small feeble premature girl. He also quotes a case reported by Fordyce Barker of a woman who delivered a term infant on July 10, 1855. On September 22, seventy-three days later, she delivered a term girl which was smaller than the other infant. This patient had a double uterus. These cases sound almost unbelievable and no such instances could be found in recent literature. This is readily understandable, since the modern obstetrician is not handicapped by the conventions of the eighteenth and early nineteenth century. At the present time if multiple pregnancy is not recognized before labor, it is certain to be discovered at the time of delivery. If delay in the birth of the second fetus takes place, steps are taken to accomplish this artificially. I know of only one case where the birth of the second twin was separated from that of the first by as much as twenty-four hours, an instance described by F. H. Holden.[17] Frequently twins vary in size and development. This is conventionally ascribed to difference in fetal nutrition. However, in 1920 Schaab[18] describes binovular twins weighing 1,900 and 2,850 gm. X-ray studies showed marked difference in ossification, the smaller twin showing no ossification of the epiphysis of the femur. He concludes that their development differed by at least a month. It would be of interest to make further x-ray studies in cases of twins showing a marked variation in size. Mere difference in size should be of no importance, but difference in development is of some significance.

Making up the final group are the many instances of supposed superfetation reported among the lower animals. Jepson[19] in 1883 reported a cat giving birth to a term litter and at the same time a well-preserved rounded sac containing a three-fourth-inch fetus. No further examination was carried out on the small fetus. King[20] in 1913 reported two cases observed among 700 litters of albino rats. Both of these rats gave birth to second litters two weeks after the first. The normal duration of gestation in the albino rat is twenty to thirty days. Sumner[21] in 1916 published his observations after a long experience in breeding mice. He states that superfetation occurs in 3 per cent of the pregnant animals. He feels that many of these cases must depend on the survival of spermatozoa for weeks. He also feels certain that ovulation must occur during pregnancy. Harmon[22] in 1917 reports the accidental discovery during dissection of a possible example of superfetation in a cat. Several fetuses near term were present in the uterus, together with one very small fetus. In 1918 the same observer[23] reported a possible instance in a cow which gave birth to a term calf and a four months' fetus. Smith[24] in 1927 reported the case of a large black sow which gave birth to a litter of 4 and one month later to a litter of 10. Both litters appeared to be at term. He mentions instances previously reported in animals: (1) Kroen (1897) in a goat; (2) Lapken (1897) in a sow; (3) King (1913) in a cat; (4) Harman (1918) in a cow; (5) Hunt (1919) in a cat; (6) Marshall (1922) in a cat. He states that Kuntz reviewed most of these cases in 1920 and felt that they represented the retention and preservation of dead fetuses. He feels that neither his case nor that of Lapken can be explained on this basis. In a second paper in 1927 Smith[25] reports three instances observed in pigs and three in sheep. In one of the cases reported in the sheep he feels that the evidence is particularly strong and admits of no other explanation.

Slonaker[26] in 1934 made some very interesting and well-controlled observations. In breeding albino rats, he found that in the nonpregnant state these animals showed periods of activity, demonstrable by vaginal smears and mating tests, that corresponded with ovulation. During pregnancy which lasts for twenty-two days these periods are almost always absent. In a few animals periods of activity occurred twelve to fifteen days after coitus. These he feels must indicate ovulation during pregnancy. Two such animals were observed being kept with their mates until the twentieth day of pregnancy. The females were then isolated. In both instances the animals gave birth to an apparently normal litter twenty-two days

after the first coitus. Fifteen days later they produced a second normal litter. He feels that both cases represent instances of superfetation. This evidence presented by Slonaker is the strongest that could be found in favor of the occurrence of superfetation.

Interest in the possibility of this phenomenon was aroused by the two cases occurring in the early part of 1935. The first falls into the first variety that has been reviewed.

CASE 1.—M.S., aged thirty, married, para ii, grav. i, was seen in the Out-Patient Department at Bellevue Hospital on Jan. 4, 1935. She stated that her menses had begun at eighteen, had a twenty-three to twenty-four-day interval, and lasted three to four days without pain. She had had one previous pregnancy having been delivered at New York Hospital on Oct. 28, 1933, of twins about five weeks before the expected date of confinement. They weighed 1,580 and 2,100 gm. This pregnancy was normal except for a slight elevation of blood pressure and mild albuminuria during the latter months. Otherwise her previous history was negative. On admission to the clinic she stated that her last normal menses had occurred about October 6. Slight bleeding had occurred on the preceding day. This had occurred previously on November 7, being quite profuse for one day, and slight spotting occurring for two days following. Intercourse had occurred once in October and three times in December. On examination the uterus was found to exhibit the signs of early pregnancy which was estimated at about three months. She was advised to go home and rest in bed.

She was seen again on January 9 complaining of continued bleeding. One week later she returned with the same complaint and on the following day, January 17, was admitted to the Gynecological Service.

General physical examination was negative. Pelvic examination showed a uterus enlarged, soft and rounded, about the size of a four months' gestation. The adnexa were negative. The cervix was long, softened, closed, and blue. The diagnosis on admission was threatened abortion with the possibility of hydatid mole. She was kept under observation but continued to bleed even with complete bed rest. In hopes of emptying the uterus two series of pituitrin injections were given without success. On January 28, eleven days after admission, she was sent to the operating room and the lower cervical canal and vagina were packed with gauze. Another pituitrin series was given. Although this produced no immediate effect, about eighteen hours after the removal of the packing the patient aborted a small ovum which appeared to be about two months of age. The uterus still remained large and easily palpable abdominally but little bleeding occurred. Ten and a half hours after the first abortion she passed a perfectly formed four months' fetus complete in its sac. Five days later the patient was given a thorough examination under gas. The uterus was explored but no evidence of any congenital anomaly could be found. A few days following this she was discharged from the hospital in good condition.

The following are the pathologic reports on the two specimens:

Specimen A (Fig. 1, left) consisted of a mass of blood clot and a partially collapsed ovum measuring 8 by 5 by 3 cm. On opening the amniotic sac a small fetus was found measuring 3.5 cm. from crown to buttocks. Moderate degenerative changes were present, the head was somewhat flattened. The mouth and nose were formed. The eyes were present with very definite lower lid; upper lid not formed. The head was rather markedly flexed on the body. The upper limbs were well formed; right forearm was flexed on the arm and left forearm was extended on the arm. The chest and abdomen were well formed. Right lower extremity was well extended on the body; left leg was flexed on the thigh. The general appearance

of this fetus suggested early maceration with loss of muscle tone. The umbilical cord appeared normal and measured about 4 cm. The sex appeared to be male although this is practically impossible to determine. Section of the sac showed well-formed placental tissue lying under the amniotic membrane; this did not grossly appear to be fibrotic.

Fig. 1.—Twin A (left). Crown-rump length 3.5 cm. Grossly showed slight maceration and loss of muscle tone. Section of fetus showed complete autolysis. Amniotic sac collapsed. Placenta appeared grossly normal. Twin B (right). Delivered ten and one-half hours after Twin A. Crown-rump length 12.5 cm. Grossly in perfect condition. No sections made on fetus. Amniotic sac distended. Placenta appeared grossly normal.

Fig. 2.—Microphotograph of section of placenta of Twin A. Fibrosis of villi, degeneration of chorionic epithelium and avascularity present.

Microscopic Examination.—(Fig. 2.) Sections showed masses of decidua which in places was fairly well preserved; in other areas it showed hemorrhage and necrosis. Moderate number of polymorphonuclear leucocytes was noted throughout but in some

places appeared to be more numerous than usual. Adjacent to the decidua were numerous chorionic villi showing a well-developed double layer of epithelium in many instances although in certain villi the epithelium appeared to be undergoing degenerating change. Stroma of the villi seemed to be more fibrosed than usual in healthy living placental tissue. Blood vessels were not numerous but could be found in fair proportion of the villi; when present they seemed small but contained nucleated red blood cells. Numerous syncytial giant cells were present in the intervillous spaces. Between the decidual tissue and the placental sinuses was a well-developed layer of fibrin and necrosis. Sections through fetus showed complete autolysis.

Diagnosis: Early fibrosis of young placental tissue. Autolysis of fetus (eight to ten weeks).

Specimen B (Fig. 1, right) consisted of complete ovum 16 cm. in diameter. The placenta was concentrated at one pole but apparently still covered in part the whole sac. It was very much thinner, however, over the major portion of the sac than it

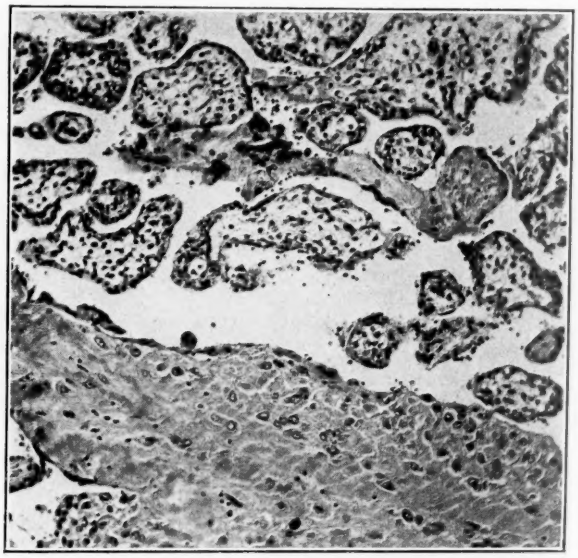

Fig. 3.—Microphotograph of section of placenta of Twin B. Normal premature placenta.

was at one pole. On opening the sac there was found a well-formed fetus 12.5 cm. from crown to buttocks. There was no suggestion in any way of maceration and the muscles suggested excellent tone. Head appeared normal. Both eyelids were formed; closed but could be separated. Nose and mouth appeared normal. Ears were fully formed. Legs were flexed on thighs. Both forearms were flexed on arms. Chest and abdomen appeared normal. Insertion of umbilical cord appeared normal, length of cord was 22 cm. and width about 0.7 cm. Sex was male. Section of placental tissue appeared normal; showed no evidence of fibrosis.

Microscopic Examination: (Fig. 3.) Sections showed well-preserved decidua containing masses of fibrin. Moderate number of polymorphonuclear leucocytes was present throughout the decidua. In certain areas these leucocytes appeared more numerous than usual. In addition, small areas of hemorrhage were present. Adjacent to decidua were numerous chorionic villi. The epithelium surrounding these villi was well preserved and for the most part consisted of single layer of cells. The covering epithelium appeared mainly of syncytial type but appeared to be undergoing

early regressive changes. Very little evidence was present of the double layer seen in early placental tissue. Stroma was quite cellular and contained numerous well-developed blood vessels which contained nonnucleated red blood cells. Moderate number of syncytial giant cells was noted in the intervillous spaces. Between the decidua and placenta sinuses there was a well-developed layer of fibrin and necrosis which was being invaded by many chorionic cells of the Langhans type.

Diagnosis: Normal premature placental tissue. Normal fetus (sixteen weeks).

The ages of these fetuses are approximate according to the relation of crown-rump length to age given by Williams.[27]

Although it was first thought that this was a true example of superfetation in the human being, after careful study it was concluded from the condition of the smaller fetus and placenta that death took place some days and probably weeks before the abortion occurred. If this is a superfetation, in order for the smaller fetus to have reached the size of an eight to ten weeks' fetus followed by retention for a

Fig. 4.—Placenta showing small rounded flattened white mass about 1 cm. in diameter situated between amnion and chorionic plate near margin at about 2 o'clock.

period of time in utero after death, the second conception must have taken place in November. According to the patient's history this is impossible. Therefore, one must decide that this specimen represents a twin pregnancy with the early death of one twin and the eventual miscarriage of both fetuses. Photographs and placental sections from this specimen were sent to Dr. George Streeter[28] of the Carnegie Institute of Washington. He agreed with this opinion.

CASE 2.—Mrs. L. C., white, aged twenty-seven, was first seen June 22, 1934. She had been married six months. Her menses had always been regular without pain, lasting four to five days with a thirty to thirty-two-day interval. She gave no history of skipping a period previously. Her last menses occurred on March 16, 1934. She had not felt sick in any way since this time but noted that a week previously (June 15) she had begun to have a slight pinkish vaginal discharge. On the day before her first visit this had become dark red. Physical examination revealed a uterus that was enlarged, rounded, and soft. It appeared to be about the size of a three months' gestation. The cervix was long, thick and closed. No bleeding was

present at the time of the examination. The estimated date of confinement was December 23. Spotting continued during July and the uterus increased in size to about that of a 4 months' pregnancy as noted on July 23. The uterus remained stationary during August, and on the twentieth a diagnosis of dead fetus was made. No further growth had taken place on September 10, in fact, the uterus seemed smaller. Intermittent spotty bleeding continued during all this time. The patient was told that the fetus was dead, and she was asked to return in two weeks. On September 24 she reported that she had felt definite movements two days before. The uterus was found to have enlarged almost to the umbilicus. Pregnancy progressed normally from this date, the patient going into labor spontaneously on Feb. 14, 1935, almost two months after the original estimated date of confinement. She was delivered by low forceps and median episiotomy of a normal male child weighing 6 pounds, 2 ounces. Inspection of the placenta and membranes showed nothing unusual in the membranes. On the fetal surface of the placenta (Fig. 4) near the margin was a small rounded flattened white mass, about 1 cm. in diameter, which lay beneath the amnion and was movable to a limited degree. Section of this mass (Fig. 5) showed a mass of rather hyaline connective tissue. The periphery was

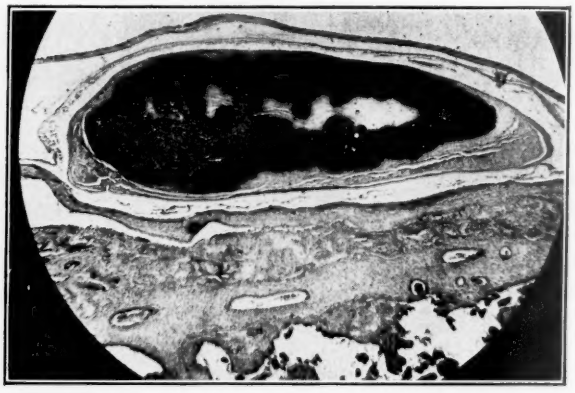

Fig. 5.—Section of small mass noted between amnion and chorionic plate. Made up of hyalinized connective tissue. Periphery filled with round or oval calcified masses.

filled with rounded and oval calcified bodies, the center was free from these. This may represent the remnants of a small calcified ovum.

Two explanations can be offered for this peculiar clinical history: One, that this patient had a sixty-day amenorrhea preceding her pregnancy; that she then had a twin pregnancy and that in July one of the twins died. The other explanation involves superfetation, the first pregnancy preceding the second by two months, and its development ceasing during the early stages of the second pregnancy. In both explanations the stationary uterus would be caused by the collapse and shrinkage of one sac and the growth of the other.

In order for superfetation to occur one must believe that ovulation, fertilization, and nidation can occur after a pregnancy has been established in the uterus for at least a month. Fertilization should be possible until about the third month when the uterine cavity is obliterated by the fusion of the decidua vera and the decidua reflexa. Transportation of the fertilized ovum to the uterus can take place and is shown to be even more rapid in the pregnant than the nonpregnant rabbit according to Snyder and Wislocki.[29] Nidation should be easy in the

extensive decidua vera for at least two months following the beginning of pregnancy. The factor on which this phenomenon rests, therefore, would seem to be the occurrence of ovulation during pregnancy.

There has long existed a strong conviction that ovulation was inhibited during pregnancy. The basis for this opinion was not discovered but, presumably, it was founded on the inactive appearance of the follicular system other than the corpus luteum during pregnancy. Certain observations are repeatedly quoted to show that in spite of this strong opinion occasionally ovulation does take place.

Christopher[30] in 1886 reported an autopsy on a pregnant cat performed near term. He found in one ovary a mature follicle ready to rupture. He concluded that this follicle must have matured during pregnancy. He quotes an observation by Pouchet in 1840 who found mature follicles in different stages of development in the ovary of a pregnant sow. He also quoted a paper by Mayerhofer in 1876 reporting 6 cases of ectopic pregnancy, the ovaries showing recent corpora lutea together with well-developed ones. The writer concluded that the early corpora lutea must indicate recent ovulation. He also refers to a case reported by Slavjansky in 1877 of a woman dying of an ectopic pregnancy, one of whose ovaries showed a mature corpus luteum, a recent corpus luteum, and a mature follicle. Consentino[31] in 1897 reported the case of a woman dying when about six months pregnant. Examination of her ovaries showed a recent corpus luteum and many follicles ranging from the primordial type to those almost mature. Rovano[32] in 1907 reported the examination of 100 ovaries obtained from pregnant women. He observed ripening follicles several times and in 5 per cent of cases a recently ruptured corpus luteum. No other references could be found after a rather hasty and incomplete search. In order to obtain an idea of the appearance of the follicular system during early pregnancy the following work was undertaken. One hundred cases of ectopic pregnancy were selected in which an ovary had also been removed. At least one section from each ovary was available and in many instances several. Examination of these ovarian sections showed primordial follicle in the majority, and frequently follicular cysts. The granulose cells lining these cysts were often small, deep staining, and to a greater or lesser degree showed desquamation into the cyst cavity. Many cysts showed partial collapse. In sixteen instances a maturing follicle was present, but in only one case did the ovum and its surrounding granulose cells appear well preserved and healthy. The chorionic villi in this case were mere shadows with no cellular structure. This completely functionless tissue could have no influence on the ovary. In the remaining cases the maturing follicle showed varying stages of disintegration. Degenerating ova, collapsing spaces, small deep staining, desquamating granulose cells were present in all. No recent corpora lutea were found. In no instance was more than one corpus luteum present. One can conclude from these findings that maturation of the ovum takes place during human pregnancy, but that this terminates in degenerative changes and atresia. No evidence could be found to suggest that ovulation actually takes place. This is in agreement with the work of Evans and Swezy[33] in their studies on ovagenesis and the normal follicular cycle. They studied the ovaries during pregnancy in the rat, guinea pig, dog, cat, and monkey. They noted series of ova developing only to end in atresia. In the rat they could find no evidence of ovulation. This point is not mentioned in the case of the other animals. It is necessary to conclude that, while maturation of the ovum takes place during pregnancy, this process ends in atresia and ovulation does not take place. The early observations which have been quoted may well represent misinterpretations. This cannot be proved without reviewing these sections which, naturally, have not been available.

In a recent paper Snyder and Wislocki[34] have shown that a physiologic inhibition to ovulation during pregnancy definitely exists. They found that in the nonpregnant rabbit the injection of 0.1 c.c. of concentrated pregnancy urine sufficed to produce ovulation. In the pregnant animal doses 20 to 40 times as great (2 to 4 c.c.) were required to obtain this result. In addition it was found that it was very difficult to produce ovulation at all during the first four days of pregnancy. Coitus occurs rarely during pregnancy in the rabbit but in the few cases observed, no evidence of ovulation could be found. Autopsy on the animals injected with these large doses after the fourth day of pregnancy showed two sets of ova. The tubal set was unfertilized, the uterine set was encountered as developing blastocysts. In no case was the second set fertilized. This, they believe, corroborates the previously mentioned work of Hammond and Ansell showing the short duration of fertility in the sperm. They succeeded in fertilizing the second set of ova by artificial insemination and recovering both sets of ova at autopsy. Therefore these observers have produced superfetation experimentally in the rabbit. Snyder[35] in 1934 published further work on artificially produced ovulation during the latter part of pregnancy in rabbits. While this work has no relation to superfetation it is mentioned because of its interest. The duration of pregnancy in these animals is about thirty-two days. Ovulation induced on the twenty-fifth day of pregnancy regularly produced one of two effects. The rabbit either aborted within one to two days a fresh unmacerated set of fetuses or carried the pregnancy past term to about the fortieth day or fifteen days from the time of injection about corresponding to the duration of the corpus luteum. The fetuses were definitely postmature.

The facts that have been outlined show that ovulation in the human being during pregnancy is unlikely. The work of Snyder and Wislocki[34] puts on a firm basis the fact that ovulation can be induced with difficulty during pregnancy in the rabbit and that a definite physiologic inhibition exists. The nature of this inhibitory mechanism is unknown but it seems more than likely that such a mechanism must exist in the human being.

In a spirit of pure speculation, may not this inhibitory factor in the human being be present in the pregnancy hormone itself? This hormone, peculiar to the human beings and the great apes, reaches its greatest concentration at the end of the first month of pregnancy or at about the time when the next ovulation should occur. The effect of the administration of large doses of this hormone on the ovary has been noted by several observers. This effect is vastly different in human beings and monkeys from that in the rodent.

Engle[36] in 1933 found that this hormone injected into macaque monkeys produced instead of follicular growth, a cessation of ovarian activity, with atresia of large follicles and hyalinization of small follicles. This result corresponds closely with the appearance of the human ovary in pregnancy. Geist[37] noted no follicular growth or luteinization but rather arrest in follicular development in ovaries obtained from patients treated with pregnancy hormone ante-operatively. Recently an ovary, obtained from a patient receiving massive doses of pregnancy hormone before operation, was examined. Marked congestion was present together with retrogressive, atretic changes in every follicle. Engle[38] feels that if pregnancy hormone produces such an effect in all likelihood it is an indirect one. He has demonstrated that the injection of pregnancy hormone produces a degranulation of the basophile cells of the anterior pituitary. In this way there is produced pre-

sumably a loss of activity of the cells producing the gonad stimulating hormone. There would seem to be some basis for suspecting that, among its many effects, this hormone, through the pituitary, depresses ovarian function and prevents ovulation during pregnancy.

CONCLUSIONS

1. No proved case of superfetation in the human being could be found in the literature.

2. A few cases were found (Longmore,[4] Schaab[18]) that suggest that this phenomenon is possible.

3. In order to prove such a case certain criteria must be filled; i.e., the pregnant woman must deliver two or more fetuses of widely differing size, appearance, and development. If the smaller fetus is born dead, the condition of this fetus and placenta must be determined by microscopic examination. Only if this fetus and placenta appear normal and healthy can such a case be considered a superfetation. Should the smaller fetus survive birth, x-ray examination of the centers of ossification might prove of value.

4. The occurrence of superfetation seems most unlikely in view of the marked inhibition of ovulation which exists during pregnancy.

5. Two cases are described which superficially suggest superfetation. One is shown to be an instance of the retention of a dead twin, the other twin remaining alive. The other is a case of prolongation of pregnancy which suggests the possibility of superfetation, but which leaves no opportunity to submit this explanation to proof.

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THE TOXEMIAS OF PREGNANCY*

IV. The Carbohydrate Metabolism

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IN PAPERS which have previously appeared the authors have considered certain of the results of an elaborate clinical and laboratory study on a group of fifty pregnant women, all of whom presented some form of the toxemias which may be associated with this physiologic state. The first paper[1] dealt with the demonstration of an hepatic factor in a very considerable portion of the group, while the second communication[2] analyzed the nitrogen metabolism before and after delivery.

The present paper deals with a survey of the carbohydrate metabolism during gestation and in the period immediately following delivery. It has long been recognized that during even normal pregnancy various indices appear of changes in the levels of sugar utilization, and naturally during the period of lactation an entirely new mechanism is in operation with the end-result of lactose synthesis presumably mediated by the mammary glands. Further, it is equally probable that the same or like agencies are concerned with the transformation of blood glucose into galactose as one essential preliminary step in the building of milk sugar. Normal performance presents a definitely different picture for the pregnant and lactating female from that offered by the adult woman in a state of sexual rest. The criteria of normality in pregnancy have already been established by investigation, and have been summarized elsewhere by one of us.[3] The principal data were derived from the observation of a series of normal women studied throughout their pregnancies and for some weeks thereafter. These figures will be drawn on freely for control material. In addition, as, in the group of conditions loosely gathered together under the general caption of "toxemia," clear-cut evidences of a renal or an hepatic pathology or both may present, similar records have been compiled from two series presenting severally these two conditions (unpublished data from other investigations) in uncomplicated forms. From comparison with them, some further light may be thrown on the mechanisms underlying the carbohydrate anomalies. Finally, a last series of studies from women with functional or organic (castration) failure

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of the ovaries has been drawn on for further control material. As one of us[4] has shown, ovarian failure closely simulates the changes in normal function level which characterize the state of pregnancy. The composition of these several series may be presented in tabular form for later orientation.

TABLE I. COMPOSITION OF SERIES

SERIES	NO.	FEMALES PER CENT	AGE, AVERAGE
A. Pregnant, toxic	50	100	30 yr.
B. Pregnant, normal	100	100	24 yr.
C. Hypogonad	300	100	34 yr.
D. Hepatic dysfunction	100	77	38 yr.
E. Cardiorenal	50	70	46 yr.

A few additional words of explanation are apposite. The relative youth of the normal series comes from the fact that many of them were unmarried mothers drawn from institutions providing for their care. The time factor necessary for the development of functional derangements operated in the ovarian failure series and even more significantly in those with the hepatic and cardiorenal conditions. The inclusion of males in these last two series was intentional, the underlying pathology in both series offering no characteristic sexual content.

There are three primary approaches to the estimation of the levels of carbohydrate metabolism, namely, the urine, the blood, and the measurement of the tolerance or utilization capacity. This last may be approached from several standpoints, such as (a) provocative melituria, (b) blood sugar curves, and (c) changes in the respiratory metabolism as recorded by the respiratory quotient, or the specific dynamic action. The first method only of this third group has been utilized in these studies. The approach through the changing levels of blood sugar under excitation of a conventional test meal lacks a sharpness of quantitative definition and entails a series of venipunctures which rapidly cools the enthusiasm of the volunteer subject of experiment. Measurement of the respiratory exchange calls for a highly skilled technical approach, is very time-consuming, and yet again lacks at the present time those clear-cut standards of normal response which prevent differences from assuming a reasonable arithmetical precision. At some future date, when enough data have been compiled to confer clarity of outline on the standards, it seems certain that respiratory measurements will become a method of election for precise study; at present, its several disadvantages outweigh the possible gain from its use.

In the categories listed above, the first named was the urine. Under normal conditions, the twenty-four-hour urine does not contain enough reducing material to give a positive sugar test with a suitable delicate reagent such as the well-known Benedict solution. Collections made

after a meal will usually give a positive test as the result of glycuresis, but this leakage through the kidney in appreciable quantities of partly unidentified reducing bodies is, at best, a transitory phenomenon and the accumulations at these periods are so diluted in the complete twenty-four-hour collection as to render the latter negative to conventional qualitative testing. The appearance of sugar in detectable amounts in such a twenty-four-hour collection is to be regarded as abnormal and an evidence of disturbance in the carbohydrate metabolism. That such abnormality is the end-result of a myriad of not necessarily related causes is too well recognized today to require more than passing comment. The urine findings in the several groups under consideration have been collected in Table II.

TABLE II. GLYCOSURIA (TWENTY-FOUR-HOUR COLLECTIONS)

GROUP	STATUS	URINE + PER CENT	COMMENT
A. Pregnant, toxic	3 to 9 mo., a.p.	16	Glucose
	10 to 14 days, p.p.	50*	Glucose Lactose
B. Pregnant, normal	4 to 9 mo., a.p.	18	Glucose
	14 days, p.p.	82	Lactose
	6 mo., p.p.	80	Lactose
C. Hypogonad	–	25	Glucose
D. Hepatic dysfunction	–	18	Glucose
E. Cardiorenal	–	6	Glucose

*Average duration of pregnancy
+ = 8.7 months
0 = 7.8 months

During the period before delivery, the incidence of glycosuria is substantially the same in both the toxic and normal pregnant women. The normal figure here is somewhat higher than the usual report; our studies call for repeated examinations (over 700 in this group), a fact which explains the seeming discrepancy. Fourteen days after delivery, 82 per cent of the normal pregnant women show lactose in the urine; this is patently the common finding and presumably represents no more than a combination of overproduction coupled with the limited capacity of the organism to utilize this sugar when the integrity of the disaccharid molecule is unimpaired.

Turning to the toxic group, the incidence of melituria postpartum is appreciably lower than in the normal group. Further analysis of the detailed data of each case shows that the positive group were approaching normal term at the time of termination of the pregnancy. On the other hand, the negative series contain a number of cases with early miscarriage or therapeutic abortion, the pregnancy terminating before the mechanism of lactation had been established. Naturally, individual cases vary, this no more than the normal and anticipated fluctuation of physiologic function, but the relative duration of the two groups as given in the table offers a reasonable explanation for

the lower incidence of postparturient melituria. The differences in the urine sugar in the two groups are another confirmatory evidence. The persistence of lactose even up to six months postpartum has already been recorded. The group of ovarian failures, in which condition a depressed sugar tolerance is a characteristic sign, exceeds the influence of pregnancy to an appreciable degree, and the liver cases show a parity with the first two groups. The occasional appearance of glycosuria in cardiorenal cases associated with hypertension was reported by O'Hare[5] in 1920, and his findings confirmed more recently by several others. The underlying mechanism of this phenomenon need not concern us at this time. It should be noted, however, that lowered renal permeability may also and in opposite sense affect the passage of sugar through the kidney as well as of the several nitrogenous constituents of the blood which usually form the focus of attention in this condition.

To summarize the urine evidences in relation to our thesis, it may be said that toxic pregnancy shows no greater incidence of glycosuria during its progress than does the normal course of this physiologic state. Further, emptying of the uterus before the termination of gestation seems to influence favorably a return to the normal, at least so far as the disappearance of melituria is concerned. The postpartum lactosuria is to be regarded as a physiologic rather than pathologic manifestation and appears alike in the toxic and the normal.

How far blood sugar levels are competent to indicate disturbances in carbohydrate metabolism is a very real question. True, there are a few conditions such as diabetes and hyperpituitarism on the one hand, and adrenal failure and insulin shock on the other, that exert influences on blood sugar that the normal homeostatic agencies cannot control. On the other hand, there are a great variety of more or less morbid states in which sugar utilization is gravely disturbed and yet which give no evidence in significantly changed levels of blood sugar. Departures from the conventional norm, for this reason, assume a wholly special significance.

The averages for this quantity derived from the several series are grouped in Table III.

TABLE III. BLOOD SUGAR

GROUP	PARTUM	
	ANTE-	POST-
A. Pregnant, toxic		
I, II, III	84	90
IV	88	96
Total, average	85	92
B. Pregnant, normal	83	94
C. Hypogonad	97	
D. Hepatic dysfunction	93	
E. Cardiorenal	96	

A few words of explanation are required. Groups I, II, and III in the toxic series all had established or probable hepatic factors in the etiologic complex. Group IV alone of these subdivisions gave no objective evidence of a liver complication. This might account for the somewhat higher value both ante- and postpartum which offers a modest contrast to the other antepartum levels. That pregnancy produces low normal blood sugars is a well recognized fact. So strong is this influence that in a group of patients studied actually after labor was well under way,[6] the average for the group was 82 mg., in other words, slightly, and not significantly, below the lowest level recorded here. The quick recovery postpartum to normal levels coupled with the equally normal averages of the other control groups offers convincing evidence that the low normal blood sugar of pregnancy is a phenomenon intrinsic in the physiologic status and disappears once the exciting cause is removed by emptying the uterus.

To summarize the blood evidences briefly, toxemia in the pregnant woman produces no change in the blood sugar levels which would differentiate these several states from that of normal gestation.

Turning next to the third, and in some ways the most decisive of the evidences of the level of carbohydrate metabolism, we consider the approach by provocative melituria. The selection of sugar for the test meal is a question of primary importance. For many years past, one of us has been studying the utilization of galactose in man in a wide variety of physiologic and pathologic states. In a similar manner, we are now investigating levulose by the same methods and in the same wide scatter of normal and abnormal physical conditions. The third common hexose, glucose, has as yet not been included in this program of study, since it is less well adapted for certain types of approach than are the other two. For one reason alone, the normal tolerance is so high that its verification by the administration of the test meal to the fasting patient not infrequently produces gastrointestinal disturbances that drastically terminate the test. Its use in those conditions where tolerance is actually increased produces an augmentation of the initial difficulty and appreciably lowers the percentage of successful tests.

The highly controversial topic of tolerance testing as such need not be discussed further as the present thesis is concerned solely with the presentation of certain objective results obtained under sharply defined conventions of performance. Briefly, the sugar is administered to the fasting and resting patient, usually at 7 A.M. and after the collection of a two-hour control urine. Subsequent two-hour urine collections are made at 9 and 11 A.M., and all are tested qualitatively for the presence of reducing material. In event of a positive response, the amount present is quantitatively determined. In galactose testing, if the control specimen shows the presence of glucose, the subsequent

collections are freed by fermentation before final examination is made. The levulose approach is rather more elaborate in that the urines are tested by the Selivanov reagent and the fructose when found to be present is quantitated by a combination of several methods including the use of the precision polariscope. As the analytical procedures here employed as well as a number of others have been subject to extensive critical analysis, the results of which are shortly to appear, further discussion may be waived at this time.

In the series of normal pregnant women constituting the present first control group, the galactose tolerance was determined at stated intervals, usually one month, throughout the pregnancy. Likewise, after delivery, the practice was continued for as long a period as contact was maintained. These results have already been published[3] but the table may be reproduced here for purposes of orientation.

TABLE IV. GALACTOSE TOLERANCE IN PREGNANCY

PERIOD	MONTH	TOLERANCE DOSE		
		20 GM.	30 GM.	40 GM.
Antepartum	3	67%	33%	0
	4	67%	33%	0
	5	63%	37%	0
	6	67%	33%	0
	7	62%	38%	0
	8	89%	11%	0
	9	100%	0	0
Delivery				
Postpartum	1*	100%	0	0
	2	73%	27%	0
	3	100%	0	0
	4	67%	33%	0
	5	25%	75%	0
	6		50%	50%
	over 6			100%

*Third and fourth weeks only.

There is a steady progressive fall of galactose tolerance toward an inferior level 50 per cent below the normal, which latter is shown by all of the cases in the series during the last month. After delivery, recovery begins in the second and is usually complete by the expiration of the sixth month. It is interesting that this recovery takes place irrespective of the lactational status of the mother.

Before discussing the results of applying this test to the several groups, it may be briefly stated that the tolerance dose, i.e., that which will produce a transitory trace of the sugar in the urine while a dose ten grams less yields only negative results, varies somewhat with the sex and with the sexual status of the individual. The present series are confined to adults, hence the normal male tolerance of 30 gm., and that of the female of 40 gm. applies to all of the members of the several groups with the exception of the pregnant, whose levels have already been recorded in Table IV. The collected data are given in the next table.

TABLE V. GALACTOSE TOLERANCE

GROUP	STANDARD NORMAL	OBSERVED TOLERANCE		
		DEPRESSED	NORMAL	INCREASED
A. Pregnant, toxic				
antepartum	20-30	25%	64%	11%
postpartum	20-40	42%	56%	2%
B. Pregnant, normal				
antepartum	20-30	0	100%	0
postpartum	20-40	0	100%	0
C. Hypogonad	40	100%	0	0
D. Hepatic dysfunction	30-40	91%	7%	2%
E. Cardiorenal	30-40	46%	52%	2%

Brief analysis of the data shows the following:

As the study of the normal pregnant woman defines the normal response to the sugar, the 100 per cent record is inevitable. The ovarian failure cases all show a depressed galactose tolerance as one of the many diagnostic points, the summation of which defines the underlying etiology. The hepatic group, as might well be anticipated, shows a dominant downward tendency. A few normal cases are recorded, and two of the series show that rare condition of an increased tolerance which has already been recorded elsewhere.[7] The cardiorenal group shows a downward tendency, the incidence of depressed tolerance being in excellent agreement with the figures of O'Hare[5] already noted. The single case with an increased level showed a significantly lowered renal permeability to which fact this anomalous result is probably attributable.

Turning now to the toxic series, a very real scatter of results appears. This presumptively does no more than express the algebraic summation of the several factors of influence which these patients exhibit. Two-thirds are normal ante- and one-half postpartum. The abnormal responses are generally in the direction of a lowered tolerance. Several antepartum and one patient after delivery, however, show the anomaly of an increased utilization capacity. Further detailed analysis of this group is given in the next table. As this analysis calls for the use of the four subgroups already noted, they may be briefly defined.

In Group I, an hepatic factor was objectively demonstrated and a renal element denied with equal authority. Group II showed both hepatic and renal involvements by objective methods of approach. In Group III, the hepatic element was probable but lacked final confirmation; renal abnormality was excluded. In Group IV, as already noted, there was a renal but no liver component.

In the antepartum period, the liver factor causes a significant deviation from the normal in nearly half the cases. After delivery, the normal moiety is substantially unchanged but practically all of those departing from this standard show a depressed tolerance. With Group

IV, the uncomplicated renal fraction, less than one-fourth of the patients depart from the normal during the antepartum study but nearly one-half show depression after the termination of gestation. Interpretation of these findings, at best, must be highly tentative in the light of our present knowledge. The liver cases of the first three subdivisions show a shift from the antepartum scatter toward a consistent depression in those cases which are abnormal. Conceivably this is a

TABLE VI. GALACTOSE TOLERANCE; ANALYSIS OF TOXEMIA GROUP

GROUP	BELOW 20	20-30	OVER 30
	1. Antepartum		
I, II, III	29%	58%	13%
IV	15%	77%	8%
	2. Postpartum		
I, II, III	41%	56%	3%
IV	45%	55%	0%

residuum of the earlier liver abnormality expressing itself consistently with a further or sustained lowered level of hepatic function. With Group IV, the residual damage is relatively greater and produces only depression.

The only warrantable general deduction to be made from these figures is that toxic pregnancy produces marked changes in the galactose metabolism. This is in striking contrast to the urine and blood reports and must be conceded to be far more consistent with the known physical status of the members of the toxic group.

Turning to the levulose metabolism, it becomes necessary as a preliminary step to define standards of the normal. Our work with this sugar is still under way and all of the indications with it lack that clarity of outline which the galactose figures possess as a result of the application of the test to nearly five thousand completely studied individuals. Recognizing that our figures at this time must be tentative and possibly subject to future revision, the best criteria now available are given in Table VII.

TABLE VII. NORMAL CONTROLS, LEVULOSE (VALUES ARE APPROXIMATE)

STADIUM	FEMALE	MALE
Prepuberal	75	100
Puberal	75-100	
Adult	100-125	

The sex difference with galactose, reported so frequently in earlier papers, does not find a certain parity when this second sugar is used. Our best figures for the adult female seemingly lie between 100 and 125 gm. for the tolerance dose; the adult male is seemingly positive with 100, although here too there may be a possible slight upward

trend. Until numbers confer more authority on proposed standards, we prefer to record limits, as has been done above, and then report observations in absolute rather than relative terms. Once standards are established, these records can be readily translated into terms of deviation.

The values for the normal and toxic pregnant woman are given in the next table, using this convention. Here, too, the series are brief, and larger numbers will presumably modify the absolute arithmetical magnitudes. We doubt, however, if they will significantly change the trends here recorded to any considerable degree.

TABLE VIII. LEVULOSE TOLERANCE IN PREGNANCY

DOSE	ANTEPARTUM		POSTPARTUM	
	NORMAL	TOXIC	NORMAL	TOXIC
25	0	17%	0%	7%
50	44%	38%	27%	52%
75	22%	38%	55%	27%
100	34%	7%	18%	7%
Over 100				7%

Considering first the normal group, one finds one-third of the series falling within the range tentatively assigned to the healthy woman in a state of sexual rest. One-fifth show a depression to the level similarly ascribed to childhood, while nearly half are below this boundary which, with galactose as the test sugar, forms the limit of normal depression. The postpartum figures show a tendency toward concentration at the 75 gm. level, although significant representation is recorded in the moieties both above and below.

Turning to the toxic series, it is evident that the whole trend is downward. For example, 17 per cent are at a level (25 gm.) lower than any of the normal group. Further, while two-thirds of the normals are positive with 75 gm. or less, 93 per cent of the toxic cases fall within this range. After delivery the same tendency is manifest, both in the 7 per cent still positive with 25 gm. and in the concentration of half of the group at 50 gm. instead of the 75 gm. level of the normal series. Toxicity certainly lowers the utilization power of the pregnant woman for levulose but scarcely to a degree that might be inferred from her double burden nor yet with a certainty that admits of no exception. Broadly speaking, levulose follows the trends already noted with galactose but in a qualitative rather than a quantitative sense. Further, there are certain lacks of correlation between the evidences with the two sugars that emphasize the differences probably intrinsic in the individual mechanisms of utilization.

One more line of approach may be attempted in an effort to sharpen the clarity of the indications with this sugar. Expressing tolerances in terms of the averages of the positive doses for the several groups

and supplementing the two pregnant series with the figures from other small groups drawn from the current levulose studies, we have the data collected in Table IX.

TABLE IX. ANALYSIS OF LEVULOSE TOLERANCE

GROUP	SUBGROUP	AVERAGE + DOSE		
A. Pregnant, toxic		A. P.		P. P.
	I	58		75
	II	59		75
	III	60		50
	IV	61		61
	Total, average	59		65
*B[1]. Pregnant, normal		72		73
*C[1]. Hypogonad			91	
*D[1]. Hepatic dysfunction			80	
Normal adult tolerance†			100-125	

*Small series of 15 to 35 cases.
†Approximate value.

The toxic groups certainly show average values below those of the pregnant series. In subgroups I and II of the toxic cases, those in which a liver factor was established, there is recovery on delivery to levels on a parity with the normal postpartum figure. This, by the way, is one of the interesting lacks of correlation with galactose, already noted above. The other two do not reflect this improvement, Group IV being unchanged and Group III experiencing a still greater depression.

The ovarian cases do not show that depression with levulose that is so striking a feature of their response to galactose. They are a little low, it is true, but by no means reach the levels determined by pregnancy. Finally, the liver cases show a downward trend less marked than in the response to galactose. With the usually postulated influence of the liver on levulose metabolism, this is interesting; it remains for confirmation with a larger series for the observation to assume meaning.

The material here presented scarcely calls for formal summary as each section has been briefly interpreted in the course of the discussion.

One may say that simple blood and urine evidences fail to indicate true disturbances of carbohydrate metabolism in toxic pregnancy other than those intrinsic in the common physiologic condition. By tolerance testing, however, both with galactose and levulose, there is an unmistakable downward trend from the levels of normal pregnancy to those reported in the toxemias. The indications, however, lack a clarity of outline and definition which permits of an arithmetical expression. Certainly with levulose, less precisely as regards galactose, the trends are qualitative rather than quantitative. Superimposed disturbances of carbohydrate metabolism in the toxic group are, however, demonstrated with certainty.

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BEHAVIORAL CONSEQUENCES OF CEREBRAL BIRTH LESIONS*

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FORTUNATELY, the hazards of birth, for both mother and child, have been greatly reduced by modern programs of prenatal care and increased attention to obstetric details. The number of children injured at birth is remarkably small in the face of the possibilities for morbid consequences. Adequate statistics are not available, but probably less than three surviving children per thousand are seriously affected by congenital palsy, and probably less than one-third of these are also mentally subnormal.

Some of these "injuries" are the result of developmental anomalies or maternal diseases during pregnancy. Others are due to imperfect or incomplete development of the child at birth. In still other cases anatomic or physiologic complications in the mother endanger the infant beyond the protective limits of modern obstetric skill. The attending physician carries a heavy burden of responsibility even in an uncomplicated delivery. That these responsibilities are discharged with the utmost fidelity, and with ever increasing skill and concern, is witnessed by the relatively small number of untoward consequences in the face of the many difficulties encountered.

There are many types of organic nervous lesions in childhood which produce mental subnormality or motor paralysis. Among these, the neuromuscular incoordination of intracranial birth palsy is fairly distinctive, yet not very generally differentiated for purposes of treatment. Formerly thought of as orthopedically hopeless, these "spastics" have lived their isolated lives as helpless burdens. More recent knowledge discloses that the mental condition of such children is more commonly hopeful than hopeless, and their physical handicaps of speech and movement do yield to well-considered orthopedic treatment.

*Read at a Symposium on Birth Injuries for the Philadelphia Obstetrical Society, November 7, 1935.

The earliest work on congenital palsies in children was done just a hundred years ago. It is usual, however, to date the recognition of this condition from about 1840, when William J. Little, an English orthopedist, described in some detail the mental and motor consequences of lesions of the brain at the time of birth. The condition has since generally been known as "Little's Disease," the most obvious symptom of which is generalized impairment of voluntary musculature.

One of the first in this country to call attention to the behavioral consequences of birth injuries in children of school age was Dr. Walter S. Cornell, Health and Medical Inspector of the Philadelphia schools, who wrote in 1912:

"Injuries of the head at time of birth . . . produce an unknown number of mental deficients. . . . How many of the simply dull and backward school children arise from this cause cannot be determined."

Dr. Cornell's early description of infantile cerebral paralysis produced by head injuries still provides a good description of this condition. He says: "This disease . . . presents a paralysis resulting from injury to the brain. This injury usually occurs during a difficult labor, particularly if obstetric forceps be required, but it may occur from inflammation of the brain substance or rupture of a cerebral blood vessel during the first few years of life. The cause of the latter event is usually unknown. After recovery from the first shock of fever, a permanent paralysis remains, affecting usually one side of the body and often including one side of the face. In such cases, it is equivalent to an ordinary stroke of apoplexy occurring in childhood. In other cases both sides are paralyzed, so that the whole body is affected. In a few cases both lower limbs only are paralyzed. There is no marked wasting of the paralyzed limbs, although contractures and deformities develop. The paralyzed muscles show evidence of nerve irritation, and the tendon reflexes, such as the knee jerk, are exaggerated. For the same reason the hands and face often show spasmodic movements when used for manual work or speech. Since the brain is the part actually injured, it is natural that not only paralysis but a feeble mind, may ensue, and from a practical standpoint these cases are classed as mental disease. It is therefore very important to distinguish between spinal and cerebral paralysis. In the former, intelligence is normal, the paralysis is usually only in one limb, the tendon reflexes are absent, and there is more wasting of muscles."

The immediate consequences of birth injuries are evident chiefly in the production of motor handicaps. Mental deficiency is a frequent accompaniment of these handicaps. Or mental retardation may result from birth injury, without serious motor handicaps. There is some reason to believe that disturbance of personality may also be produced by birth injury, independently of motor handicaps or mental retardation. Sensory handicaps, especially of sight and hearing, may be still other consequences involving, particularly, muscular disturbances in the visual apparatus.

The motor disturbances provide the most conspicuous symptoms in these cases. These include, particularly, spasticity and athetosis. Spasticity is defined as "simultaneous and hypertonic contractions of antagonistic muscle groups of the voluntary motor system." These muscle groups act reciprocally in such a way that, normally, as one muscle group contracts the corresponding or antagonistic group relaxes. Spasticity reflects the simultaneous rather than the reciprocal action of these

groups, such that the corresponding movement is performed only with difficulty and with consequent delay.

Athetosis, on the other hand, reflects an interference of involuntary movements superimposed upon fairly well-coordinated voluntary movement. The intended movement is therefore disturbed by irrelevant muscular activity, often accompanied by "overflow" into functionally unrelated muscle groups. This is apparently produced by an imperfect selective action of the different muscle groups and results in poor control, with fairly rapid movement.

Mental subnormality frequently accompanies the motor handicaps which arise from birth injuries. It should be emphasized, however, that normality of intelligence is more common than subnormality. Indeed, there are many instances of striking superiority of intelligence in spite of the most severe physical handicaps. The expression of intelligence is rendered so difficult by the motor handicaps that the mental ability of these patients is often seriously underestimated. Moreover, the motor difficulties often prevent the early expression of an underlying mental capacity, so that the intelligence does not become functionally expressive until relatively late in life. Consequently, it is of the utmost importance that adequate mental examinations of these patients be made as early as practicable, in order to separate the mentally retarded from the mentally unaffected for purposes of education and training.

In contrast with those individuals who show severe paralysis without mental retardation, there are undoubtedly many mentally retarded children whose condition is due to birth injuries which do not produce accompanying motor disturbances. Recognition of these cases is difficult because the neurologic basis of the mental retardation cannot be demonstrated by present examination methods. Undoubtedly, many cases of idiocy, and probably many instances of milder degrees of mental retardation, could be traced to injuries at the time of birth if examination methods and the interpretation of history data were more precise. In the absence of motor symptoms these children are not easily distinguished from the ordinary feebleminded.

There is good reason to suppose that birth injuries which affect the motor and intellectual systems may also produce disturbances of personality. It has been demonstrated that disturbances of behavior resembling psychopathic conditions are very commonly associated with histories of abnormal birth, and enough is known of the anatomy and physiology of personality to strongly suggest a presumptive relation between difficult birth and abnormal behavior.

At present we know of no reliable statistics regarding the frequency of birth injuries and their relation to mental subnormality. This is because the conditions at birth which might produce abnormalities of development cannot safely be assumed. It is necessary for diagnosis that

there also be evidence in the child that the abnormalities of delivery did actually affect him adversely. These effects are noted in the condition of the child at birth or soon thereafter, as indicated by deficient animation, convulsions, abnormal reactions of infancy, motor disturbance, intellectual apathy, and the like.

The mental and physical consequences of abnormal birth become more clear as the development of the child proceeds. Retardation in the development of motor functions and in expressive behavior during infancy tend to confirm the likelihood that the child was actually injured at birth. If there is mental retardation or disturbance of motor functions, the history should show that this may not have been due to some postnatal pathology, such as accident, disease, and the like. Heredity should also be free from suspicion. There are many conditions whose symptoms resemble those due to birth injuries and the final impression as to both symptoms and cause must be left to competent medical diagnosis.

In a careful survey at The Training School at Vineland, New Jersey, it was found that about 10 per cent of 450 mentally deficient children owed their condition to cerebral birth lesions. This condition seems, therefore, numerically second only to unfavorable heredity as a cause of mental deficiency.

At the Spalding School, Chicago, about 450 out of about 900 crippled school children are classed as "spastics." Most of these cases are probably due to cerebral birth lesions. One-third of these are rated as mentally subnormal, but this may be a rather high estimate, due to the difficulties of early mental diagnosis in such children.

Thus we may say: (1) if one person per 100 is feebleminded, and if one-tenth of the feebleminded are birth-injured, then one person per 1,000 is feebleminded due to this cause; and (2) if seven children per 1,000 are crippled, and if one-half of these are spastic, and if one-third of these in turn are mentally deficient, again we would find one person per 1,000 with mental deficiency due to birth injuries. These figures are, however, only tentative.

The possibilities of education and training among children suffering from birth injuries are of special importance. First, however, the condition must be adequately diagnosed with reference to both mental and motor symptoms, and perhaps with reference to personality disorders as well.

The most promising method of treatment of the motor difficulties is muscle training administered by skilled physical therapists under the direction of a competent orthopedic surgeon. If the child is mentally retarded, it is rather likely that muscle training will prove less promising than if he is mentally normal. Adequate recognition of the mental condition is, therefore, of the utmost importance. For this purpose, it is necessary that the psychologist conducting the mental examination in

consultation with the physician be familiar with the clinical mental symptoms of birth injuries. He must also be especially skilled in the administration and evaluation of mental test procedures, and in the use of history data in collaboration with the orthopedist or neurologist. The motor handicaps of these subjects render mental examination especially difficult. Speech is very commonly affected and this, combined with the handicaps of manipulation, greatly limits the application of standardized mental tests that can be properly applied. The examiner must guard against being so sympathetic that he interprets the test results too liberally, and yet must be sufficiently alert not to penalize the child unduly for handicaps of expression. The mental prognosis must consequently be guarded and successive examinations will be needed to confirm the impression regarding intellectual development.

Whether mentally normal or subnormal, these patients are of particular interest to the special class teacher in the public schools. There is always some possibility that the apparently subnormal child with motor handicaps due to birth injuries may prove to be mentally normal. One serious problem is to discover such unsuspected ability and overcome the motor handicaps by instruction through special methods of education. If the child is receiving muscle training, it is of the utmost importance that such training be correlated with educational methods so that the motor progress can be capitalized for expressive purposes. Education must therefore provide motivation which is essential for increasing the child's confidence in his own abilities in spite of his neuromuscular limitations.

In spite of the apparent helplessness of these children, astonishing results can sometimes be obtained and the teacher will be encouraged by the enthusiasm and progress of the pupil. The results of such training are often so extraordinary, and so obvious, that they provide a powerful incentive for further effort, giving the teacher something of that compensation which the physician experiences as his patient progresses through the successive stages of convalescence. The most optimistic teacher tends to underrate the capabilities of birth-injured subjects. She often obtains unexpected results which lead to more enthusiastic effort.

A hundred years of observation, investigation, treatment and training of birth-injured subjects has brought us to a point where new light is shed on the conservation of these exceptional children in the public schools. The current interest in crippled children, and the experiences gained in training mentally subnormal children, provide an exceptional opportunity for the birth-injured child. Perhaps no class of handicapped children presents more difficult problems of remedial instruction. Yet no single group of children appeals so much to our sympathy and holds so much promise as these.

And what of prevention? P. Brooke Bland suggests a five-point program:

First, adequate prenatal care. This involves not only the hygiene and physiology of pregnancy, but also adequate forecast of the possible dangers likely to confront the expectant mother at the time of delivery.

Second, the competent management of the delivery, with a minimum of operative procedures and a maximum of patience (the "masterly inactivity" of good obstetrics), but recognizing that a properly assisted delivery may be less hazardous to both mother and child than merely letting nature take its course.

Third, immediate exercise of spinal tap in all newborn infants where there is a suggestion of possible brain hemorrhage, whether in an apparently normal spontaneous delivery or in a complicated labor.

Fourth, repetition of spinal tap, if necessary, until spinal fluid is reasonably clear of the products of hemorrhage.

Fifth, administration of maternal blood (or other suitable adult blood) to avoid further hemorrhage.

If, in spite of these precautions, damage is done, there is a reasonable hope that at least some of the effects will be overcome through the processes of growth. Early, persistent, and long-continued programs of muscle training, supplemented by judicious use of special therapy and educational methods will go far toward helping the child to attain a happy and useful, if not wholly competent, place in the world about him.

DISCUSSION

DR. P. BROOKE BLAND, PHILADELPHIA, PA.—Statistics disclose that each year, in America, 150,000 babies are stillborn or die shortly after delivery. This means, roughly, the death of one baby every three minutes throughout the 365 days of the year.

The study made by Holland, as well as by many other investigators, indicates that intracranial damage with hemorrhage is not only one of the chief causes of the lamentably high fetal mortality, being responsible for from 20 to 40 per cent of stillbirths and neonatal deaths, but likewise in many instances for tragic and disabling sequelae of the cerebrospinal system.

A study of the problem in our own clinic discloses that in 5,442 consecutive births there were 258 deaths (a fetal mortality of 4.75 per cent). Of these deaths, 36, or 10.08 per cent, were due to intracranial injury with hemorrhage.

There are, I realize, two schools deeply interested in the problem, one claiming that intracranial injuries do, and the other that injuries of this character do not, result in destructive changes in the brain and spinal cord. To me, the latter assumption seems unwarranted.

In adults, hemorrhage about the Rolandic fissure, for example, is always followed by disabling sequelae both early and late. These resemble strikingly the complications arising from intracranial damage of the newborn child. In the adult, injury of the vital contents within the cranium, especially when accompanied by an outpouring of blood, is always followed by degenerative changes in the brain. Is it not logical to assume that similar changes should take place in the newborn child?

NEONATAL MORTALITY*

A Review of Four Hundred and Twenty-Eight Deaths

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DURING the past several years many contributions have appeared based on the maternal mortality of various hospitals and cities, and the profession has been much exercised about the possibilities of a reduction of this mortality. Much less attention has been paid to fetal deaths and their causes, notwithstanding the fact that the birth rate of this country and other countries is approaching the death rate.[1, 2] With babies at a premium, it is the duty of the obstetrician to determine, whenever possible, the cause of the fetal death, and to reduce as far as is humanly possible neonatal mortality.

There are two ways in which the obstetrician can combat the falling birth rate. The first is to reduce the pain of labor so far as is consistent with the safety of the mother and child, and the second is to lessen the incidence of fetal mortality. An increase in the number of surviving children will help to offset, to some extent, a falling birth rate.

In this analysis of the stillborn and neonatal deaths taken from one hospital, there will be no attempt to compare the mortality of this hospital with that of others, or with that of the community in general. Various factors tend to make such comparisons of dubious value. The rate would vary in different hospitals depending upon the number of syphilitic patients handled, the proportion of colored to white, the type of prenatal care, and the number of emergency cases transferred to the hospital. Indeed it is well to keep in mind that, "Statistical inquiries perhaps are frequently viewed with more respect than may actually be warranted. When applied to medical subjects, statistics have the same significance as the x-ray: they are a means to an end, not an end in themselves. Thus the now numerous statistical studies dealing with maternal mortality must be analyzed as a laboratory test would be rather than serving merely as a basis for recriminations. The lesson of essential importance is not that the maternal mortality rate is higher in one country or district than another but that some of them may be favorably affected by the knowledge gained from statistical analysis."[3] It is hoped that this analysis will, in a small degree, be a means to an end, the end being a reduction of neonatal mortality, and the means here, a possible increase in our knowledge of the factors causing infant mortality.

*Thesis presented for admission to Fellowship in the American Association of Obstetricians, Gynecologists and Abdominal Surgeons at the Forty-Eighth Annual Meeting, Skytop, Pa., September 16 to 18, 1935.

A few words about the type of material comprising these cases. More than half of the cases are private, delivered for the most part by men doing general practice. The rest are clinic patients, the great majority of whom have had prenatal care. These clinic patients usually come from the vicinity of the Hospital and are from a class of people, on the whole, somewhat higher from the financial and other aspects, than those patients attending clinics in large municipal institutions. The frequency of syphilis as a cause of neonatal mortality is, in this group, quite low. Clinic patients with positive Wassermanns are referred elsewhere. The number of patients referred from the outside lies probably somewhat between that of the municipal institutions, which are to some extent "dumping grounds," and that of strictly lying-in hospitals, practically all of whose cases come from their own indoor or outdoor clinics. Colored patients are a negligible factor in this analysis. No attempt will be made to list the deaths according as to whether they were stillborn or lived any length of time, as it is felt that a much better classification is afforded in a different manner. It is, for example, from the standpoint of etiology, a matter of little importance in a case where a child died of cerebral hemorrhage, whether the hemorrhage was produced before it was born so that a stillborn child resulted, or whether the baby managed to survive two hours or two days after the trauma.

The analysis includes those patients delivered at St. Elizabeth's Hospital, Brighton, Massachusetts, from 1927 to 1934 inclusive. During this time there were 6,149 children, and there were, including those that were not viable, 428 deaths, triplets occurring twice and twins in ten instances, a fetal mortality then of 6.9 per cent. There were, however, 23 nonviable babies, and if we subtract this group it gives a corrected mortality of 6.6 per cent.

The causes of deaths are listed in the order of their frequency of occurrence, and taken up in detail.

1. a. Chronic nephritis, 40 b. Toxemia of pregnancy, 30 c. Separated placenta, 16	86	20.1%
2. Cerebral hemorrhage Definite, 54 Probable, 12	66	15.4%
3. Monstrosities	42	9.8%
4. Prematurity	37	8.4%
5. Asphyxia	32	7.47%
6. Infection of newborn	26	6%
7. Nonviable	23	5.6%
8. Placenta previa	15	3.5%
9. Hemorrhagic disease of the newborn	9	2.1%
10. Rupture of the uterus	4	0.9%
11. Congenital heart disease	4	0.9%
12. Thymus (possible)	3	0.7%
13. Atelectasis	2	0.4%
14. Miscellaneous	4	0.9%
15. Cause of death obscure	75	17.5%

1. The following three types of cases have been grouped together, viz., toxemia of pregnancy, chronic nephritis, and separated placenta. This is done only because it is impossible, from the data at one's disposal, to determine in many cases whether a case was one of toxemia of pregnancy or nephritis; and it was also impossible to determine because of lack of data, just how many of the cases of separated placenta were toxic. Inasmuch as we know now that most cases of the latter show definite signs of toxemia, it has been thought best to place these under one classification and subgroup them. There are altogether 86 cases in this classification (20.1 per cent of the total). (a) Of these, chronic nephritis was responsible for 40. All except 3 of these were stillborn children, and these 3 were premature. Nearly all started in labor spontaneously. (b) Toxemia of pregnancy accounted for 30 cases. Of these, 5 had convulsions. Eight may have been nephritic. Nearly all these patients started in spontaneous labor. (c) There were 16 cases of separated placenta. In 14 cases the child was stillborn. In one of these cases the patient was definitely a chronic nephritic. One child lived one day, another died in three days. One of the babies in this large group was autopsied.

2. *Cerebral Hemorrhage.*—There were 54 cases that were definitely cerebral hemorrhage and 12 where cerebral hemorrhage was the probable cause, which gives a frequency of occurrence of 15.4 per cent. The following facts emerge from a study of these cases. Only 7 of these were normal deliveries, and it is interesting to note in these that of the 7, 3 were premature deliveries and 2 were twins, both of which are factors that increase the chances of cerebral hemorrhage. There were only 5 cases of low forceps deliveries, 2 being performed on premature babies. Mid-forceps operations were performed 6 times, and high forceps in 19 instances. Version and extraction were done 17 times. It should be noted that in only 6 of these versions was the operation elective; in the other 11 cases forceps were tried and failed. Moreover of the 6 cases of version and extraction, when the operation was elective, 1 was a case of prematurity and hydramnios, another a toxemia of pregnancy where the child which died was one of twins. There were 8 cases of breech extraction, 1 being premature and 1 a twin pregnancy. Cesarean section was performed 2 times, but in both following futile attempts at delivery with forceps. In 2 cases the type of delivery is not noted. Frequently the diagnosis placed in the record was that of asphyxia or congenital heart disease but the type of delivery, difficulties encountered, and where the child lived, its subsequent course, made the diagnosis of cerebral hemorrhage unquestionable. Many of these children were stillborn, dying during the process of delivery. Toxemia was a factor only three times and prematurity six times. The majority of these patients were primiparas, and the cause of the difficulty was disproportion. Some of these patients were referred from the outside after futile attempts at delivery, but the majority were handled from the beginning of their labor in the hospital, either privately, or in the clinic. X-rays were taken infrequently, and then usually on the service cases, but not the private patients. Consultation, when held, was usually held after the patient had been in labor a long time and generally when attempts at delivery had failed. Autopsies were performed in only two instances. Of the two autopsies that were performed, the first case was a normal delivery, the child living two and a half hours and the diagnosis being congenital heart disease. Autopsy however revealed a hemorrhage at the base of the cerebellum and atelectasis. The second case that was autopsied was a personal case. The labor was premature by a month, low forceps delivery was performed and greater traction was needed to deliver the baby than expected. The baby had a pallid asphyxia and died in several hours, autopsy revealing hemorrhage at the base of the brain.

3. *Monstrosities.*—These occurred in forty-two cases, about 9.8 per cent of the total. Syphilis was not a factor in any of these. There was no history of previous abnormalities, and where subsequent deliveries took place there was no repetition

of the disaster. Most of the children were of the anencephalic type, oftentimes with spina bifida and club feet. Hydrocephalus occurred a few times, microcephalus once, and there was one cyclops, and one sympus apus or congenital lack of the extremities. Nearly all of these, of course, were stillborn, a few living for a short while. There were no autopsies.

4. *Prematurity.*—There were thirty-seven cases. Prematurity was then the cause of the loss of 8.4 per cent of the babies. Definite factors were responsible for one-third of these premature deliveries. Twins accounted for ten cases, triplets for two, and one was a case of ovarian cyst which was operated. In the rest there is no factor which was obvious, except for the fact that in three cases there were previous histories showing a tendency to spontaneous premature labor. Many of these cases were terminated by low forceps, a fact about which some comment will be made later. Of these premature deliveries two were delivered by cesarean section without preliminary x-rays. One of these had had a previous repair of an old tear, and the second had a deformed pelvis from infantile paralysis.

5. *Asphyxia.*—There were thirty-two cases (7.47 per cent). (a) Fifteen of these were cases of prolapsed cord, all but one being stillborn. Of these fifteen cases, placenta previa was the cause of malpresentation in two instances, and in two other cases, the shoulder was the presenting part and the cause of the prolapse. One of the cases was referred from the outside. It is not obvious from a perusal of these cases how the prolapse of the cord could have been prevented. One child lived seven hours and autopsy revealed marked hemorrhage of the adrenal gland, a common autopsy finding. (b) There were five cases in which difficulty in delivery of the shoulder was the cause of death. These patients were all delivered by house officers, and they were all very large babies, one baby weighing 14 pounds, 4 ounces. Autopsy was performed on one of these babies and revealed complete atelectasis. (c) In two cases the cause of asphyxia was knotting of the cord. (d) There were five cases in which labor was prolonged, the child dying during the labor before any attempts at delivery. One of these cases was autopsied and revealed marked edema of the pia arachnoid. (e) In one case the cord was coiled tightly twice around the neck, evidently shutting off the blood supply, with resultant intrauterine death. (f) There were two cases quite interesting, where cerebral hemorrhage resulted evidently during labor, before rupture of the membranes occurred. In both of these cases the progress of labor was normal. The fetal heart sounds were regular, but following rupture of the membranes at full dilatation, a great deal of meconium came away and deliveries were promptly and easily performed by low forceps. One of these was autopsied. It lived several hours with pallid asphyxia and an autopsy revealed one large cerebral hemorrhage. The other child was not autopsied but had several convulsions and the case was clearly one of cerebral hemorrhage. They have been classified under the heading of asphyxia however, because the fundamental explanation seemed to be interference with circulation in the cord, which was wound around the neck. The case autopsied was a personal case and a careful review of all the factors seems to leave no explanation but that of cerebral hemorrhage resulting from intrauterine asphyxia due to shutting off of the circulation in the umbilical cord. (g) There was one case of breech delivery where the cord was extremely tight between the legs, and it was felt that this was the cause of asphyxia. (h) Another child was delivered covered with foul mucoid material and the physician was unable to clear the air passages of this. The origin of the mucoid material is obscure. The child lived three-quarters of an hour. The diagnosis was atelectasis. Autopsy was performed in four cases in this group. Adrenal hemorrhage occurred in one, cerebral hemorrhage in another, marked edema of the pia in the third, and in the fourth where a house officer had delay in extraction of the shoulders, atelectasis.

6. *Infection.*—There were twenty-six cases (approximately 6 per cent). All of these of course died after delivery. The average length of life was seven days. Two facts stand out. There were sporadic cases of children dying of pneumonia, infected throats, etc., but the majority of these deaths occurred either in 1928 or 1930, at which times there were epidemics of infection in the nursery. Bronchopneumonia, or diarrhea, with high temperatures were the clinical findings in these infants with the exception of two which had infection of the throat and middle ears.

7. *Placenta Previa.*—This accounted for fifteen cases (3.5 per cent). Nearly all of these naturally were premature. One was autopsied. This was a personal case. The baby lived several hours, showing pallid asphyxia. Autopsy revealed a tremendous amount of cerebral edema.

8. *Hemorrhagic Disease.*—There were only nine cases. In one of these there was clinical evidence of cerebral hemorrhage but there was also generalized bleeding. This group then accounted for 2.1 per cent of the deaths. The routine injection of whole blood subcutaneously in the newborn is not done in this hospital. Of these nine cases two were breech, two were forceps and five were normal deliveries. In one of these nine the diagnosis of hemorrhagic disease is questionable, the clotting time being seven minutes and bleeding time four minutes, with a difficult midforceps delivery, the baby weighing six pounds, five ounces. Of these nine cases one patient had a toxemia of pregnancy and the baby that died was one of twins. Another patient had nephritis and labor was induced with a bag.

9. *Rupture of the Uterus.*—There were four cases (0.9 per cent). One was a postmortem cesarean section. A previous cesarean had been done. Another rupture occurred after prolonged labor, before the patient was sent to the hospital. In a third there was a transverse presentation which caused a rupture during labor, and the last was that of a bicornuate uterus which ruptured before labor. Three of the mothers died.

10. *Congenital Heart Disease.*—There were four cases (0.9 per cent). This diagnosis was often made when the facts did not seem to warrant it. Of these four cases, one was premature, in another the mother already had one child which had congenital dislocation of the hip and club feet, and one mother had a positive Wassermann.

11. *Thymus.*—This gland was responsible, possibly, for three deaths. One was stillborn. Autopsy revealed a thymus weighing twenty grams. Another child died in four days, beginning to have attacks of cyanosis on the third day. Autopsy was negative except for moderate enlargement of the thymus. The third child had attacks of dyspnea and cyanosis from shortly after delivery. The pediatrician diagnosed the case as one of enlarged thymus gland. There was no autopsy.

12. *Atelectasis.*—There were of course many cases where the lungs showed at autopsy atelectasis, or where the clinical diagnosis of atelectasis would be justified but they were placed in other groups because, from the standpoint of etiology, the diagnosis of atelectasis was insufficient or misleading. There were two cases (0.4 per cent). One however was a breech delivery in which there was pallid asphyxia and the question of cerebral hemorrhage of course cannot be ruled out. The other was a large baby delivered without difficulty by low forceps, but the lungs never expanded properly, and cyanosis was present until death.

13. There were several cases not capable of being grouped in the previous classification. There was one case of syphilis, another of intestinal obstruction, one where the mother had severe pernicious anemia and delivered a stillborn, and the last where a child deeply jaundiced at birth revealed at autopsy enlargement of the spleen and liver and a blood slide characteristic of myelogenous leucemia.

14. When the cases had been grouped, there still remained 75 (17.5 per cent) where the cause of death was obscure. Nearly all these were stillborn, 54 being in

this class. In some the difficulty in ascertaining the cause of the stillbirth was due to the incompleteness of the record, but in the majority the patients had a normal pregnancy, a previous normal history, and where subsequent pregnancies followed, normal deliveries later. Moreover they had normal blood pressures, and had no signs of toxemia or nephritis. The presence of this large unclassified group indicates the necessity for autopsies in all stillborn and neonatal deaths. In two instances repeat cesarean sections were performed without previous roentgenograms. In both the babies were macerated.

COMMENT

It is obvious that in certain of these groups that there can be, with our present knowledge, no reduction of infant mortality. There are however some types where a reduction is possible.

1. *Infection.*—There are three sources of contamination of infants. One is uncontrollable. This concerns visitors to patients in the hospital, and under present hospital rules it is an important one. The controllable factors are the contacts of nurses and doctors with the infants. If the following simple rules are carried out, the possibility of infection from these two sources will be at a minimum. New nurses coming on duty should have a careful examination of hands, nose and throat, and a culture of the throat. Those showing positive *Streptococcus hemolyticus* cultures should not be allowed to handle infants, as also, of course, those who show evidence of chronic, subacute, or acute infection of the nose or throat. It should be emphasized to the nurses that they must immediately report head colds, sore throats, and infected fingers to the nurse in charge, and the infected nurse must immediately be taken off duty. Doctors should reduce examinations of newborn infants to a minimum, and when examinations are made should wear a sterile gown, be capped and masked, and should be furnished with a stethoscope from the nursery, and not allowed to use their own. Moreover the hands should be scrubbed and then rinsed in antiseptic solutions before a baby is examined. All these are important, particularly in a general hospital where men doing general work are taking care of infants. A doctor who comes from a scarlet fever case is a great menace to newborn babies unless he takes definite precautions. There should, if possible, be two nurseries alternately used, scrubbed and aired, and of course, the appearance of any discharge from the nose or eye, or skin lesion should call for immediate quarantine of that baby, and removal from the obstetric department.

2. *Cerebral Hemorrhage.*—No one who has done any amount of obstetrics feels that cerebral hemorrhage can be reduced to the vanishing point. A percentage around 12 or 15 per cent would seem high. Certainly if it could be brought home to the profession at large that consultation with the obstetrician, particularly in the case of a primipara, or one with a history of previous difficult deliveries, should be held before labor starts and not after labor has been well under way, or after futile attempts at delivery have been made, then the results would be better both for the baby and the mother. In any primipara when the head is not well engaged a few weeks before term, the use of roentgenograms will result in the saving of many more babies and the prevention of some cripples. Some of the convulsive cases in this series may have been tetanoid.

3. *Hemorrhagic Disease of the Newborn.*—The routine injection in the newborn of an ounce of blood under the skin at the time of delivery, is a simple procedure. Excellent results have been reported and it seems logical.

4. *Prematurity.*—In many cases of prematurity in this series, forceps deliveries were performed or breech extraction, and occasionally version and extraction. It cannot be too strongly emphasized that whenever possible a delivery should be normal. The performance of a generous episiotomy in a primipara who is in premature labor

and the expression of the child by abdominal pressure without the use of instruments should help to reduce the incidence of cerebral injuries in these delicate infants.

5. *Bleeding Cases.*—Whenever it is felt that the blood supply of the child has been interfered with, either by internal hemorrhage as in previa cases, or by interference with the circulation by abnormalities in the cord, the possibility of a marked cerebral edema as the cause of the asphyxia should be kept in mind, and if a spinal tap shows fluid under increased pressure, some infants may be saved. The only sign present in these infants may be pallid asphyxia. There may or may not be bulging of the fontanels, and convulsions and cyanosis are not necessarily present.

6. *Large Babies.*—The loss of five infants in this series simply because the babies were very large and the house officers were not competent to deal with the situation should lead to the institution of a rule that every large baby should be reported to the visiting obstetrician so that these unnecessary deaths may be avoided.

7. The presence of such a large unclassified group points to the necessity of very careful clinical records, and also the necessity for postmortem examination in all neonatal deaths including the stillborn. Apart from the possibility of an increase in our knowledge as to the cause of death in these cases, it is easier to obtain autopsies on infants than adults, and the obstetrician can be of service to the pathologist of the hospital in raising the percentage of autopsies.

8. The existence of thymic death in the newborn is not definitely proved from this study. This is in agreement with the findings of Hudson.[5]

The writer wishes to express his appreciation to the Reverend Thomas J. Brennan, superintendent of the hospital, Charles Kickham, M.D., chief of obstetrics, and to Sister Elizabeth Marie, librarian, for their assistance and cooperation, and to the members of the staff for permission to include their private cases.

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476 COMMONWEALTH AVENUE

SURGICAL COMPLICATIONS IN PREGNANCY*

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IN SURGICAL complications during pregnancy the conservation of both maternal and fetal life must influence us in our decisions. Where life or health of the mother is at stake, we believe that the maternal welfare takes precedence over that of the fetus. Usually elective operations should be deferred until after delivery. Pregnant women are subject to *most* of the surgical complications that may call for intervention.

Mussey and Crane pointed out that 2 per cent of the women presenting themselves for surgical lesions at the Mayo Clinic over a period of several years were pregnant. Baer, Reis and Arens stated that of 1,700 appendectomies on adult women, 1.7 per cent of them were pregnant. Paddock reported that 2.5 per cent of the series that he reviewed were pregnant.

*Read at a meeting of the Chicago Gynecological Society, November 15, 1935.

It is quite evident from the literature and also from the hospital records of some patients operated upon during pregnancy, chiefly by general surgeons, that the pregnancy was not diagnosed or at least not recorded. Hence, we believe that the incidence of surgery done in pregnancy is greater than statistics in general seem to indicate.

It is our impression from this study, although we have no comparable statistics to prove the point, that surgical complications of certain types, viz., traumatic surgery, occur less frequently during pregnancy than in the nonpregnant woman. The explanation of this difference may be due to the exercise of caution on the part of the patient and to her prenatal attention.

Though pregnancy may add to the gravity of the complication, nevertheless the clinical findings of an emergency make the picture primarily surgical. Better surgical technic, improvement in anesthetics and in methods of giving them, with proper preoperative and postoperative consideration of the existing pregnancy, have removed many former actual risks to mother and fetus.

This report includes a survey of the surgical complications occurring in 9,767 consecutive patients with uterine pregnancies admitted to the Obstetrical Service of the Presbyterian Hospital and to the Outpatient Department of Rush Medical College of the University of Chicago. I am reporting only those patients operated upon and disregarding those presenting surgical complications not demanding surgical intervention. The latter group is included in the preceding report by Dr. Edward Allen and Dr. Carl P. Bauer dealing with the medical complications of pregnancy in this same gross group of patients.

Of the 9,767 patients studied, 72 were operated upon. No attempt has been made to include dental surgery, removal of infected teeth or other foci of infection, or other minor surgical procedures not later discussed. The service as a group has felt for years that these conditions, particularly foci of infection, play a greater rôle than is ordinarily supposed. This is borne out by our analysis of the medical complications of pregnancy. We have now instituted a method by which these so-called minor complications may be more accurately evaluated, and we hope to report the results at a future date.

Table I lists the complications and number of operations performed in these various surgical procedures. The complications are listed in the order of their frequency.

In Table II we have divided the fibromyoma uteri into four groups with respect to the gestation period and the type of operative procedure performed.

The first group includes those patients operated upon by myomectomy and the pregnancy allowed to progress.

In the second group treatment was postponed and myomectomy done at the time of delivery by cesarean section at or near term. It is of

interest to note that the morbidity and days of postoperative hospitalization are noticeably increased by this procedure as compared to the results of Porro cesarean section for a similar condition.

TABLE I. OPERATIONS IN 9,767 CONSECUTIVE OBSTETRIC PATIENTS

	NUMBER	MISCARRIAGES	MATERNAL DEATH	LIVING CHILD	REMARKS
Fibromyoma					
Early myomectomy	5	1	0	3	1 not yet delivered
Cesarean + myomectomy	5	0	0	5	
Porro cesarean	13	0	0	13	
In puerperium	2	0	0	2	
Urinary tract	9	0	0	9	
Ovary	9	1	0	8	
Appendix	6	0	0	6	
Thyroid	4	1	0	3	
Breast	4	0	0	3	1 not yet delivered
Hemorrhoids					
In pregnancy	3	0	0	3	
In puerperium	4	0	0	4	
Bartholinian gland	3	0	0	2	1 not yet delivered
Bowel	2	0	1	2	
Hernia	2	1	0	1	
Incarcerated uterus	1	0	0	1	
Total	72	4 or 5.5%	1 or 1.39%	65	3 not yet delivered

TABLE II. FIBROMYOMA UTERI

AGE	PARITY	GESTATION	TREATMENT	MATERNAL MORTALITY	DAYS IN HOSPITAL	MISCARRIAGES	LIVING CHILD
30	0	10 weeks	Myomectomy	0	20	0	+
36	0	12 weeks	Myomectomy	0	33	After 2 weeks	0
38	i	14 weeks	Myomectomy	0	14	0	+
25	0	18 weeks	Myomectomy	0	15	0	+
30	0	16 weeks	Myomectomy	0	14	0	Now 6½ months
35	0	Term	Myomectomy + cesarean	0	20	0	+
36	0	Term	Myomectomy + cesarean	0	13	0	+
28	0	37 weeks	Myomectomy + cesarean	0	26	0	+
38	0	Term	Myomectomy + cesarean	0	25	0	+
42	0	Term	Myomectomy + cesarean	0	20	0	+
13 patients		At or near term	Porro cesarean section	0	Average 15 days		Living child in each case
Para iii		12th post partum day	Vaginal hysterectomy	0	Left on 24th postpartum day		
Para ii		14th post partum day	Posterior colpotomy	0	Left on 22nd postpartum day		

Two patients with fibromyoma uteri were treated by operation during the puerperium; one by vaginal hysterectomy because of persistent bleeding, the other by posterior colpotomy draining an abscessed fibroid in the posterior culdesac.

In a group of eight patients (Table III) only two patients required major operative treatment; one a right ureterolithotomy, the other a nephrectomy for hydronephrosis and stricture of the right ureter. The remaining six patients were treated by cystoscopy with ureteral catheterization at the gestation period indicated in the chart.

All of these patients had ovarian cysts (Table IV); only two were operated upon before viability of the fetus. One of them aborted twenty-four hours after removing a simple cystoma in an eight weeks'

TABLE III. URINARY TRACT DISORDERS

AGE	PARITY	CONDITION	WEEKS OF GESTATION	TREATMENT	FATE OF FETUS
28	i	Right stone, pyelitis	16, 24, 28	Cystoscopy, ureteral catheter	Term delivery
26	0	Pyelitis	26	Cystoscopy, ureteral catheter	Term delivery
26	0	Pyelitis	28	Cystoscopy, ureteral catheter	38 weeks' delivery Living child
30	0	Pyelitis	28	Cystoscopy, ureteral catheter	36 weeks' delivery Living child
27	i	Pyelitis	30	Cystoscopy, ureteral catheter	Monstrosity at term
32	ii	Right stone, pyelitis	30-40	(6x) cystoscopy, ureteral catheter	Term delivery
30	iii	Right stone	24	Ureterolithotomy	Term delivery
27	i	Right hydronephrosis, stricture ureter	16	Right nephrectomy	Term delivery

TABLE IV. OVARIAN TUMORS

AGE	PARITY	TUMORS	WEEKS OF GESTATION	FATE OF FETUS	LIVING CHILD	MATERNAL MORTALITY
27	0	Left simple cystoma	8	Miscarried after 24 hours	0	0
25	i	Twisted right corpus luteum	16	To term	+	0
28	0	Twisted hydatid Morgagni	37	Delivery after 24 hours	+	0
31	ii	Left simple cystoma	38	Delivery after 40 hours	+	0
40	0	Bilateral dermoids	Term	Cesarean, supravaginal hysterectomy	+	0
36	i	Left simple cystoma	Term	Low cervical section	+	0
35	iii	Right dermoid	Term	Porro section (fibroids)	+	0
24	0	Twisted right simple	6th postpartum day			0
35	0	?	Term	Not operated	+	0

pregnancy. The other, operated upon at sixteen weeks, went to term. The remaining patients were operated upon between the thirty-seventh week and full term, with the exception of one from whom the cyst was removed on the sixth postpartum day. Living viable children were delivered in all these latter cases.

In a tabulation of the appendicitis cases (Table V), two patients had acute suppurative appendices that had not ruptured. All were closed without drainage.

TABLE V. APPENDICITIS

AGE	PARITY	WEEKS OF GESTATION	FATE OF FETUS	LIVING CHILD	MATERNAL MORTALITY
28	i	7	Delivery at term	+	0
23	0	12	Delivery at term	+	0
24	0	18	Delivery at term	+	0
23	i	20	Delivery at term	+	0
34	0	24	Delivery at term	+	0
31	ii	38	Delivery 40 hours postoperative	+	0

The incidence of appendectomy in this series is low as compared with the report of Baer, Reis and Arens, Mussey, and others. In spite of this apparent paucity of material, it is noteworthy that in none of these patients was operation delayed so long that ill results occurred either to the mother or to the fetus. Furthermore, our postmortem records do not reveal any deaths from ruptured appendix in pregnancy or in the puerperium.

Most of our patients with thyroid disease (Table VI) have been treated conservatively either by medical procedures or by therapeutic doses of x-ray. Four out of thirty-six patients were operated upon.

TABLE VI. THYROID DISEASES

TYPE OF THYROID	BMR	AGE	PARITY	TIME OF OPERATION	FATE OF FETUS	MATERNAL MORTALITY	LIVING CHILD
Large colloid	+17	30	ii	6 weeks	Term delivery (twins)	0	++
Toxic adenoma	+66	38	i	8 weeks	Term delivery	0	+
Toxic adenoma	+43	29	0	12 weeks	Term delivery	0	+
Toxic adenoma	+72 to +58	34	0	32 weeks	Twins (death in utero)	0	0 0

NOTE: All except first patient had had Lugol's and bed rest preoperatively; all were treated by subtotal resection.

There was no maternal mortality either in those handled by medical or surgical methods. It is interesting to note that out of the total number of thyroid disease cases studied there were three sets of twins. Two of these sets occurred in the four patients operated upon. This brings up the question of fetal mass and body surface on the increased activity of the thyroid or the consequent glandular imbalance produced by multiple pregnancy.

In one of these patients the basal metabolic rate was only +17 per cent and operation was done for pressure symptoms produced by a large colloid goiter. The other patient with twins exhibited a marked increase in rate up to +72 per cent and a toxic adenoma was removed after preliminary medical management.

Only two of the remaining operations (Table VII) had any effect upon the immediate maternal or fetal mortality rate. One patient seen

TABLE VII. MISCELLANEOUS OPERATIONS

	AGE	PARITY	WEEKS OF GESTATION	FATE OF FETUS	MATERNAL MORTALITY	LIVING CHILD
Breast Lipoma (axillary)	22	i	4th day post-partum		0	
Carcinoma left	31	0	28 weeks	Term delivery	0	+
Carcinoma right	38	?	?	Not yet delivered	0	
Accessory mammary gland	?	ii	28 weeks	Threatened premature labor 3 times, term delivery	0	+
Hemorrhoids	34	iv	28 weeks	Term delivery	0	+
Hemorrhoids	28	i	24 weeks	Term delivery	0	+
Hemorrhoids	30	ii	24 weeks	Term delivery		
Hemorrhoids (4 cases)			At delivery		0	
Bartholinian abscess	25	0	14 weeks	Term delivery	0	+
Bartholinian abscess	23	0	16 weeks	Term delivery	0	+
Bartholinian abscess	?	0	16 and 20 weeks	Not yet delivered	0	
Carcinoma sigmoid colon	43	iv	28 weeks	Delivered 72 hours post-operative	+	+ lived 1 day
Carcinoma rectum	?	iii	8 weeks	Term delivery	0	+
Right indirect inguinal hernia	23	i	24 weeks	Term delivery	0	+
Ventral hernia	37	?	8 weeks	Aborted 8 hours post-operative	0	0
Incarcerated uterus	34	0	13 weeks	Term delivery	0	+

first in the seventh month had carcinoma of the sigmoid colon complicated by bowel obstruction. A colostomy was done and the patient died on the third postoperative day. A fetus delivered a few hours before her death lived for twelve hours. Another patient had a resection of the rectum and colostomy. An eight weeks' pregnancy was not diagnosed at the time. She carried the pregnancy to term and delivered normally.

One abortion occurred in an eight weeks' pregnancy forty-eight hours after the repair of a large ventral hernia.

CONCLUSIONS

1. The maternal mortality resulting from surgery in pregnancy is 1.39 per cent in this series. This corresponds with Mussey's report of 370 cases with a maternal mortality of 1.08 per cent (Table VIII).

TABLE VIII. MORTALITY

	GROSS FETAL MORTALITY	MATERNAL MORTALITY
Allen and Bauer		
Normal	1.87%	0.0085% (1 in 1200)
Medical complications	3.7 %	0.0356% (1 in 250)
Surgical complications	5.5 %	1.39% (1 in 72)
Mussey's series of surgical complications (350 cases)	4.5 %	1.08% (1 in 92)

2. The operative mortality in pregnancy is only slightly increased over that in the nonpregnant state.

3. Gross loss of fetal life in this series is 5.5 per cent. Mussey reported 4.5 per cent. Our gross fetal mortality in women with medical complications is only slightly lower or 3.7 per cent. These figures may be contrasted with the rate of 1.8 per cent in our normal series.

4. We agree in general with the conclusions previously arrived at in the literature that hesitation and procrastination in surgical decisions should have no more place in the pregnant than in the nonpregnant woman.

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Talamo, Pasquale: A Rare Case of Myxolipoma of the Vulva, Arch. di ostet. e ginec. **42:** 635, 1935.

A tumor the size of a filbert nut was noticed in the right labium majus at five years of age. Eight years later it had reached the size of a turkey egg. Excision was simple and microscopic examination showed the tumor to be a lipoma with areas of myxomatous tissue scattered through it, a myxolipoma.

WM. PIERCE.

THE INFLUENCE OF MEDICAL DISEASES ON OBSTETRIC AND FETAL MORTALITY*

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THIS report represents a critical study of 9,696 consecutive uterine pregnancies. We have divided these cases into three groups for comparison. The first group consists of women not afflicted with medical or surgical diseases. The second group is composed of patients suffering with medical diseases. These medical diseases we have classified according to the classification proposed by Adair and Stieglitz in their recent book on *Obstetric Medicine*. The third group represents individuals affected with surgical complications. These complications will be presented by Dr. Fred O. Priest.

Table I represents the termination of the 9,696 consecutive uterine pregnancies covered in this study.

Table II is a gross comparison between the obstetric outcome of 6,007 women not afflicted with medical or surgical disease and 3,358 patients afflicted with medical diseases. Some of the noteworthy comparisons shown in this table are,

TABLE I. TERMINATION OF PREGNANCY

Term births	8,773
Premature births (viable to thirty-eighth week of gestation)	592
Spontaneous abortions (conception to sixteenth week)	53
Incomplete spontaneous abortions	194
Therapeutic abortions	37
Therapeutic abortions and sterilization	22
Miscarriages (sixteenth week to twenty-eighth week of gestation)	25
Total	9,696

TABLE II. GROSS COMPARISON OF THE OBSTETRIC RESULTS BETWEEN NORMAL PATIENTS AND PATIENTS WITH MEDICAL DISEASES COMPLICATING THEIR PREGNANCIES

NORMAL PATIENTS—6,007			PATIENTS WITH MEDICAL DISEASES—3,358	
		PERCENTAGE		PERCENTAGE
Term	5,696		3,077	
Premature	311	5.4	281	9.1
Gross fetal mortality	111	1.8	116	3.7
Afebrile	5,704	95.0	3,040	90.9
Febrile	303	5.0	318	9.1
Maternal deaths	4	1 in every 1,501 deliveries	11	1 in every 305 deliveries
Normal delivery	5,357		2,902	
Gross operative delivery	650	10.8	456	13.9

*Read at a meeting of the Chicago Gynecological Society, November 15, 1935.

first, that there are approximately twice as many premature births, stillbirths, and febrile puerperiums in the medical disease group as in the nonmedical; second, five times as many maternal deaths resulted per thousand deliveries in the medical disease class as in the nonmedical; third, the operative incidence is 3.1 per cent higher in the affected than in the normal group.

Table III is a more detailed study of the obstetric results occurring in the various medical disease divisions. It is apparent that more maternal deaths occurred when pregnancy was complicated by anemia, infected teeth, organic heart dis-

TABLE III

	TERM	PREMATURE	GROSS FETAL MORTALITY	AFEBRILE	FEBRILE	MATERNAL DEATHS	NORMAL DELIVERY	GROSS OPERATIVE DELIVERY
Anemia (below 70% hemoglobin, 3,000,000 R.B.C.)	1,139	153	36	1,136	154	3	1,000	292
Infected teeth	1,051	51	28	1,044	58	3	1,064	38
Toxemias	311	32	32	301	42	1	273	70
Organic heart disease	102	12	7	108	6	2	94	30
Syphilis	107	17	5	110	14	0	119	5
Varicose veins	208	9	3	202	15	0	212	5
Upper respiratory disease	46	0	0	39	7	0	44	2
Diseases of lungs and pleura	10	0	1	2	8	1	5	5
Skin	9	0	0	9	0	0	9	0
Thyroid disease	30	2	2	29	3	0	24	8
Diabetes mellitus	9	1	0	9	1	0	8	2
Allergic diseases	10	0	0	9	1	0	8	2
Infections of urinary tract	16	1	1	12	5	0	15	2
Gonorrhea	10	0	0	9	1	0	8	2
Diseases of body mechanism	5	0	0	5	0	1	5	0
Diseases of nervous system	8	2	0	9	1	0	6	4
Tuberculosis	6	1	1	5	2	0	4	3

ease than by any other medical complication. However, one maternal death occurred in the toxemias, disease of the lungs and pleura, body mechanism, incomplete abortions and therapeutic abortions. Fetal mortality is noticeably increased when the mother suffers from toxemia or organic heart disease. Anemic patients seem to require obstetric operative procedures more frequently in the conduct of their labor. We suggest that this may be due to inability to complete labor spontaneously because of lowered vitality. The toxemias and the anemias also seem to lower resistance against infection, since these two complications claim the greatest percentage of febrile puerperia. Premature births occurred more frequently in the anemias, toxemias, and syphilis (Table V).

TABLE IV

	WARD 51	WARD 50	WARD 41
	NORMAL OBSTETRIC	AFEBRILE, PATHOLOGIC OBSTETRIC AND MEDICAL OBSTETRIC CASES	SEPTIC AND VENEREAL OBSTETRIC CASES
Total births	8,897	2,557	2,089
Stillbirths	108	253	160
Infant deaths	79	195	144

The greatest cause of postnatal fetal death during 1933 at Cook County Hospital was prematurity indicated by the following figures: Total deaths 130, premature deaths 97, and full-term deaths 33.

Table IV graphically substantiates the effect of these diseases on premature birth and consequent fetal mortality as reported by Dr. Parmalee at Cook County Hospital.

TABLE V

DEATHS IN 6,007 NONMEDICAL CASES	DEATHS IN 3,358 MEDICAL CASES
1. V. W., aged forty, para v; 5 forceps deliveries; all stillbirths; elective low cesarean section at term. Death fourth day postpartum, peritonitis. Culture: *Staphylococcus aureus* and diphtheroids.	1. A. R., aged 34, para v. Decompensated heart. Death third day. Postmortem mitral, aortic and tricuspid endocarditis.
2. M. L., aged 25, primipara; dystocia; classical cesarean section. Intestinal obstruction. Death sixth day.	2. A. S., aged twenty-nine, primipara, midforceps. Mitral stenosis and fetal asphyxia. Death ninth day, lobar pneumonia.
3. S. G., aged 19, primipara; low forceps. Death 5 hours. Coroner's report: status lymphaticus.	3. C. C., aged 31, para iii, entered hospital temperature 102°, ruptured membranes, double footling; douche taken 14 hours before delivery. Death fourth day. Postmortem septic infarcts lungs, peritonitis.
4. M. K., aged 23, primipara; spontaneous delivery. Death twenty-sixth day, puerperal sepsis; spontaneous perforation ileum postpartum.	4. V. B., aged 40, primipara; attempted version; shock, death. Postmortem uterus intact.
	5. C. B., aged 17, primipara; dystocia, classical cesarean section. Death twelfth day, peritonitis, streptococcus and *B. coli*.
	6. P. N., aged 38, para x; placenta previa centralis, classical cesarean section. Death eighth day, pulmonary embolism postmortem.
	7. M. P., aged 22, primipara. Normal delivery; 5 large apical abscesses. Death thirteenth day, streptococcus peritonitis.
Not Classified	8. M. G., aged 32, para ii; bag induction, spontaneous labor. Death fourteenth day, puerperal sepsis.
1. Criminal abortion, sepsis and death.	9. L. C., aged 38, primipara, died during forceps delivery; ether; no autopsy.
	10. M. M., aged 35; para viii; precipitate delivery, convulsion immediately following delivery, death. Toxemia.
	11. M. R., aged 36, multipara. Precipitate labor, unrecognized ruptured uterus, retroperitoneal hematoma. Death 36 hours. Ankylosis hip joint, tuberculosis?
	12. Hyperemesis gravidarum, refused interruption until 10 hours before death.

Table VI is a summary of the essential features of all the maternal deaths. One-fifth of the maternal deaths were due to medical diseases. Death from sepsis is more frequent when pregnancy is complicated by medical ailments.

TABLE VI. ABORTIONS

	SPONTANEOUS	INCOMPLETE	THERAPEUTIC	THERAPEUTIC AND VAGINAL STERILIZATION	MISCARRIAGES
	53	194	37	22	25
Dilatation, curettage	0	194			10
Maternal death	0	1	1	0	0
Tuberculosis			2	2	Spontaneous 24
Heart disease			11	4	Induced 1
Toxemia			8	5	
Dementia precox			4	0	Complete 15
Psychosis			0	8	
Diabetes			1	2	
Pernicious vomiting			3	0	
Hyperthyroid			3	0	
Pyelitis			2	0	
Encephalitis			1	0	
Epilepsy			1	0	
Leucemia, myeloid			1	0	
Syphilis			0	1	

CONCLUSIONS

1. From this study it seems that it is five times more dangerous for a woman affected by medical disease to bear children than it is for a healthy woman.

2. The child born to a woman suffering with a medical disease is twice as apt to be a stillborn as a child born to a normal woman.

3. The increased susceptibility to infection of these debilitated women is noteworthy. One-half of these women who died, died from sepsis.

4. It is evident that future statistical studies of maternal and fetal deaths should include a critical analysis of the patient's health as a great factor in the end obstetric results, rather than basing these conclusions entirely upon the outcome of operative obstetric procedures.

5. Attempts to reduce fetal and maternal mortality should be directed toward improving the health of the expectant mothers and eliminating, as far as possible, those patients physically unfit for childbearing. This combined with improved obstetric procedures should help us to approach the irreducible minimum of maternal and fetal death.

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DISCUSSION

DR. FRED L. ADAIR.—In all we have had 41 deaths in something over 13,000 deliveries at the Chicago Lying-In. In 26 of these, associated with the pregnancy, death was due in 10 cases to infection, in 8 to hemorrhage, in 3 to hyperemesis, in 3 to embolism, in 1 to eclampsia, and in 1 to aspiration pneumonia. In this same series of 26 cases, 7 had other complications which contributed to the death; for instance, one of them had an antepartum infection which we attributed to middle ear infection. The immediate cause of death in this case, however, was postpartum

hemorrhage. Another patient who died of hemorrhage following rupture of the uterus had pyelitis and cystitis. One case of sepsis was complicated by pneumonia which, although not the decisive, was a contributing factor. Another death from sepsis occurred in a patient who, during her pregnancy, had had an operation for drainage of an appendiceal abscess. One case of hyperemesis was complicated by chronic endocarditis and another by diabetes. One of the cases of embolism had an accompanying vegetative endocarditis. Thus, out of 26 cases there were seven with serious medical or surgical complications.

Fifteen deaths occurred from complications which had nothing in particular to do with the pregnancy. In these patients the pregnancy was the complicating factor rather than vice versa. There were three cases of cardiac death; three cases of meningitis, one a tuberculous meningitis; two cases of pneumonia; and one each of agranulocytosis, diabetes, diphtheria, gonorrheal endocarditis, hyperthyroidism, nephritis, and pulmonary tuberculosis.

We could, therefore, state that 50 per cent of the deaths were affected by definite medical or surgical complications and that 15 out of the 41 deaths were definitely due to medical or surgical complications and not to the pregnancy.

DR. RALPH REIS.—We must revise our ideas that a pregnancy is complicated by appendicitis and must now consider that we have patients with appendicitis and a complicating factor of pregnancy. Ten to twelve years ago Drs. Daly and Strouse suggested that we should consider the pathologic condition as the primary disease and consider the pregnancy as the complication.

I wonder if it is advisable to regard fibroids requiring myomectomy at the time of cesarean section as being a surgical complication of pregnancy or vice versa. It seems to me those patients cannot be considered in analyzing the maternal or fetal death rate. This must also hold for patients delivered by Porro section. I would like further to raise the question of whether you consider ureteral catheterization a surgical procedure or one of simple instrumentation. If we were to take out that group and take out the group of hemorrhoids done at the time of delivery, we would find Dr. Priest's statistics to be different from those given us because there would then be 43 patients with major surgical conditions. The miscarriages would average 10 per cent and the maternal death rate would be 2.5 per cent rather than 1.3 per cent.

One other point I would like to discuss is the advisability of permitting patients with malignant disease to carry their pregnancies to term. We have felt that the burden upon the maternal organism from the effects of irradiation was too severe to permit these pregnancies to go on. Radiation lowers the blood calcium and inhibits the hematopoietic system so that a secondary anemia is produced similar to that of a pregnancy. The combination is more than any patient should be asked to bear.

DR. PHIL DALY.—There is one point upon which I am not quite clear in the consideration of medical complications of pregnancy. Are these obstetric or medical deaths?

As to anemia as a cause of increased death rate, what are the causes of anemia? May not the underlying condition which produces the anemia be really the cause of death?

I agree very sincerely with the paper as a whole, that medical conditions present during pregnancy warrant some consideration. I think the mistake has been to hesitate to treat medical or surgical complications because of the pregnancy.

DR. N. SPROAT HEANEY.—One point I wish to make is the necessity of having the patient in as good condition as possible during pregnancy by the removal of all possible foci of infection. Years ago thrombophlebitis or "milk leg" was not an unusual complication after delivery but now we find it rather rarely, due in

particular, I believe, to the cleaning up of mouths. Dr. Curtis at his clinic said that his chief surgical complication was thrombophlebitis. I do not know whether Dr. Curtis is a believer in foci of infection or not. I reported in May on 627 cases of vaginal hysterectomy for benign disease with three deaths; in these cases there was one thrombophlebitis. Since that time an additional number of patients have been operated upon so there are now 709 vaginal hysterectomies in this series still with only one case of thrombophlebitis. Except in patients coming from a distance where delay was difficult, none of these patients was operated upon until infected tonsils were removed and abscessed teeth pulled. I think that is the chief factor in the low mortality and low morbidity, and the same applies to obstetrics.

I was astounded at the number of myomectomies performed during pregnancy. It must be a rather unusual condition that would lead a surgeon to open an abdomen during pregnancy to take out myomas and leave the pregnancy intact. We know that even without pregnancy a myomectomy carries considerable morbidity and a higher mortality than does hysterectomy, so that in general, patients with fibroids should be carried along even with considerable discomfort rather than undergo operation during pregnancy.

DR. ALLEN (closing).—I think a factor behind both of these reports was self-protection. So many reports have come out in the literature as to the guilt of the obstetrician for the rising death rate in obstetrics. It may be that we have drawn faulty conclusions but it would be advisable for a similar analysis to be made of a larger group of obstetric patients so that we could divide the responsibility.

I was quite impressed in Omaha a short time ago by a report by Dr. Dannreuther of a series of 2,000 gynecologic cases; in the last 1,000 cases there was a marked difference in the final mortality that was obtained, not by perfecting surgical technic, but by paying more attention to medical complications that might affect the final result. It seems to me that instead of the obstetrician and pediatrician taking all the responsibility for this high maternal and fetal death rate, we should analyze cases with something else in mind than that the obstetrician did a high forceps and the woman died.

When Dr. Daly asked whether these were medical or obstetric deaths, a great many of them are counted against the obstetrician, but they were operated upon, that is, they had a surgical delivery, because they did not have the strength to go on. It seems to me we have been placed in a situation that should be cleared up by allocating as clearly as we can the responsibility of the patient and the various branches of medicine.

DR. PRIEST (closing).—In answer to Dr. Reis, I am not defending all the treatment carried out. The record I found on the patient with carcinoma of the rectum showed that radical resection was done and the pregnancy was not diagnosed at that time. She was not seen by an obstetrician until the fetus was nearly viable, when she came back to the clinic with swelling; the surgeon thought it might be a metastasis. Because the fetus was near viability, she was allowed to go on to term.

Myomectomy at term where cesarean section was done was included because all told most of these patients might not have had to have a cesarean at the time of delivery except for the existing complication of fibroids.

In answer to Dr. Heaney, I intended to say that two myomectomies done early in pregnancy were done with a mistaken diagnosis. An ovarian cyst was diagnosed preoperatively in one case and an ectopic pregnancy in the other. I talked to the doctor who operated upon this last patient; he did a myomectomy and had no defense for his choice of treatment done at that time.

AN UNUSUAL CASE OF POSTOPERATIVE EMBOLUS*

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POSTOPERATIVE embolus resulting in pulmonary infarction occurs frequently enough on all surgical services. The journey of the embolus from the thrombus in the vein to the lungs is a logical one and easily followed.

An embolus detached from a pelvic vein thrombus, ultimately producing death by damage in the peripheral circulation, requires much more explaining and occurs much less frequently.

Arterial emboli originating from some source in the left side of the heart or in the arteries themselves are not to be confused with the condition referred to above. For an embolus detached from a pelvic vein thrombus to directly reach the peripheral circulation certain gross developmental defects of the heart must be present, such as an interventricular septum, patent ductus arteriorsus or a patent foramen ovale. These conditions would be found at autopsy but were not found in the case under discussion.

From our autopsy findings we believe we can explain the sequence of events that occurred from the propagating thrombus in the pelvic veins to the end-result as follows: Formation of antemortem clots in both internal iliac veins. From one or both of these thrombi, very small emboli were detached, producing small pulmonary infarctions. These were not large enough in themselves to produce any subjective symptoms. In the veins draining these small infarcted areas, secondary thrombi formed and from these were detached the emboli producing the fatal accident.

Miss C. S., a fifty-seven-year-old white woman, consulted her physician because of a "feeling of weight" in the lower abdomen. She had always been well, no serious illness or operations. Menses began at about fourteen years of age, regular, recurring every twenty-eight days, and ceased about nine years ago.

Her doctor found a pelvic tumor and referred her to me for operation. Nothing was found on general physical examination to contraindicate this elective procedure. The patient led a fairly active life and continued work until the day of admission to the hospital Sept. 3, 1935.

The preoperative study showed Hg 87 per cent, R.B.C. 4,120,000, W.B.C. 10,000, polymorphonuclears 64 per cent, mononuclears 36 per cent. The urine was negative, sedimentation time was two hours and forty minutes. Blood pressure was 132/84.

Physical examination led to a diagnosis of ovarian cyst (left). The operation was on September 4, the anesthetic used was avertin 80 mil. dose and was supplemented with gas-oxygen and ether.

The tumor was found to be a simple ovarian cyst, easily removed. The appendix was also easily removed. She had a smooth convalescence, slight febrile reaction for the first three days, never over 100.2° F. and normal thereafter.

On the twelfth day after operation patient was allowed out of bed, and this was accomplished without fatigue. The next morning she again was out of bed but complained of weakness and remained up only ten minutes. She was worried and depressed about this but that afternoon she wanted to get out of bed again. This time while being aided by the nurse she became unconscious and was returned to bed.

Shortly after when seen by me there was a right hemiplegia and the left radial pulse could not be felt. The patient was inarticulate, could not swallow, and voided

*Read before the New York Obstetrical Society, November 12, 1935.

involuntarily. Examination of the left arm showed pulsation in the left axillary artery but this ceased about 1 to 1½ inches below the beginning of the brachial artery. There was no capillary reaction below the elbow, and the left forearm and hand were paler and cooler than the right.

There was evident obstruction of the brachial artery and cerebral embolus producing the hemiplegia.

Consultation with the surgeons as to the advisability of attempting to remove the embolus in the brachial artery was held, but in view of serious cerebral damage present, conservative measures were thought best. Her condition became progressively worse, and she died on the seventeenth day postoperative.

The report of the autopsy is as follows:

1. Embolus to left middle cerebral artery with left encephalomalacia.
2. (a) Bilateral pulmonary infarcts (small) and pulmonary thrombi; (b) right recent small pulmonary emboli; (c) atelectasis, partial, left lower lobe; (d) early lobular pneumonia, right middle lobe; and (e) ancient left apical pulmonary tuberculosis.
3. Diffuse, slight atheromatosis.
4. Bilateral internal iliac and common iliac venous thrombosis.
5. Left brachial artery embolus with early patchy gangrene of forearm and hand.
6. Chronic passive congestion of the liver, early.
7. Operative removal, recent, of appendix and left ovary. Recent suprapubic operative wound.

In ulnar-flexor aspect of the left forearm and left thenar eminence ovoid purplish red areas of incipient gangrene were present, some 8 and 4 cm. long by 3 and 2 cm. wide, respectively. Usual colloar-longitudinal autopsy incision.

Pericardial cavity contained 8 to 10 c.c. of straw-colored fluid. Serosa were smooth and glistening. Heart was natural in size and shape, contracted in all chambers, and contained p.m. clot and fluid blood. Endocardium was smooth. Valves and orifices were natural except for slight atheromatosis of aortic cusps of mitral valve. Myocardium was dark red, firm, and showed no scars. Foramen ovale was closed. In the right pulmonary artery two definitely antemortem, grayish red, emboli, each some 4 cm. long by 7 mm. wide, were present.

Aorta showed moderate diffuse atheromatosis with slight ulceration near bifurcation.

The left brachial artery in its first third was found to be occluded by a grayish red apparently propagated thrombus, not attached where encountered. Presumably original embolus was farther down vessel near antecubital fossa, but artery was not opened this far.

Both internal iliac veins from region of broad ligaments were found to be thrombosed, thrombus extending into common iliac veins, where in each vessel a 3 to 4 cm. grayish red, partially adherent thrombus was present. External iliac veins apparently were free of thrombi.

Pleural cavities were free of fluid and adhesions. Lungs fairly voluminous. About two-thirds of the posterior portion of the left lower lobe was atelectatic. Three centimeters' zone of fibrous and partially calcific apical tuberculosis of left lung. On section bilateral lower lobe purulent bronchitis was found; definite thick yellow pus was exuding from cut surface of bronchioles. In the right middle and upper portion of the left lower lobes red wedge-shaped infarcts of apparently the same age were present, each some 3 cm. in its widest diameter. There were a few patches of lobular pneumonia. A few thrombi were present in what were apparently pulmonary veins in infarcted zone, but careful dissection could not absolutely identify a large thrombus originating in one.

Peritoneal cavity was free of fluid. Cavity was smooth and glistening.

Liver was natural in size and shape. Capsule was smooth. On section very slight prominence of central vein zones was present. Gallbladder and ducts were natural.

Spleen, pancreas, kidneys, and adrenals were normal.

Uterus was atrophic. Right adnexa was normal, left tube slightly thickened and clubbed, but no active inflammation present. Inferior leaf of sigmoid meso was slightly adherent to site of ovary.

Left cerebrum obviously was larger than the right and its convolutions were slightly flattened. Pia-arachnoid was normal. There was very slight atheromatosis of the cerebral vessels. The left middle cerebral artery from near its origin for about 1.5 cm. was found to be completely occluded by a grayish red antemortem embolus (seemed to have been forced into vessel rather than a local thrombus).

On section there was found to be soft red infarction of lateral two-thirds of left lenticular nucleus, and of an area some 3 cm. broad by 5 cm. sagittally of anteromedial portion of left frontal lobe, involving the interhemispheral sulcus. Remainder of lobe was somewhat edematous, and the left lateral ventricle was somewhat smaller than the right. Its fluid was slightly blood tinged.

Interpretation: Apparently thrombosis of both internal iliac veins allowed small pulmonary emboli to form pulmonary infarcts, these, in turn, initiating pulmonary thrombi which gave rise to the left cerebral and brachial emboli.

Cause of Death: Cerebral embolus and left encephalomalacia. Pulmonary infarction; secondary to left oophorectomy and appendicectomy.

1168 DEAN STREET

DISCUSSION

DR. RAYMOND MILES.—This case is a relatively unusual one, but I think the sequence of events is quite clear.

The patient was a woman fifty-seven years of age whose peripheral vessels seemed to be in fairly good condition. The myocardium, grossly and microscopically, showed very little abnormal, but there was nevertheless evidence of a slight cardiac failure in the mild degree of chronic passive congestion of the liver.

It was impossible to determine from which source the emboli to the left middle cerebral artery and left brachial artery had arisen. The only question was whether the arterial lesions were thrombi locally formed, or emboli. I feel that they were emboli because the arterial walls, except for the aorta, were quite smooth and showed no signs of previous disease.

We do not know the cause of the thrombi, but this patient exhibited more of a tendency to form these than the average person, although we know that postoperative pulmonary infarctions, especially when small and often silent, are very common occurrences.

This case is interesting from a diagnostic point of view, since one must think, first, of a mural thrombosis of the left ventricle with secondary peripheral infarction; second, of a mural thrombosis, usually of the arch of the aorta; or, third, of a congenital defect in the septum of the heart or foramen ovale, allowing a paradoxical embolus to occur. The latter is the most unusual of these conditions.

DR. CHARLES R. STOCKARD.—In all such cases where there is a thrombus in a vein and, finally, an embolism in the cerebral artery, it is almost impossible, and certainly very difficult from an anatomical standpoint, to know how the embolus can get through the pulmonary capillaries into the arterial circulation. It comes up the vein, of course, into the heart and then goes to the lungs by way of the pulmonary artery. The question is: How does it get through the pulmonary vein into the cerebral artery? How can it get through the pulmonary capillaries, because that is the problem one always has to contend with in a cerebral embolism.

DR. MADDEN (closing).—We do not think that this particular embolus which became detached from the pelvic veins was the same one which finally reached the

cerebral artery. It could only reach there in the presence of some gross developmental defect in the heart. We believe in this case that the original embolus produced pulmonary infarction from which were detached the emboli which produced the fatal result.

DR. STOCKARD.—But you would have to have pulmonary breakdown.

DR. MADDEN.—You would have to have pulmonary infarction first, which was actually present in this case. Furthermore, we found thrombi in those areas from which undoubtedly arose the embolus to the brachial artery and the cerebral artery.

A CLINICAL STUDY OF THE EFFECT OF CAMPHOR-IN-OIL ON LACTATION

MILTON D. KLEIN, M.D., NEW YORK, N. Y.

(From the Obstetrical Service of the Morrisania City Hospital)

IN THE past few months, camphor-in-oil has been used on selected postpartum patients at the Morrisania City Hospital. Ninety out of 1,000 patients were studied, and it is the object of this report to summarize the clinical effects observed regarding the action of camphor on the breasts.

The effect of camphor on the breasts was first noted clinically in 1922 by J. Rosenblatt[1] who observed that when camphor was given to nursing mothers for cardiac disorders, it caused a reduction in the excretion of milk and within a few days, complete cessation of lactation. He did not offer an explanation for this action. Philpott in 1929[2] and McNeile in 1935[3] also reported that camphor-in-oil had a definite inhibitory action on lactation. Liegner[4] attempted to determine experimentally the effect of camphor on the breasts of puerperal guinea pigs whose young were weaned at birth. He observed that with camphor involution of the secretory portion of the mammary gland began on the second day and was complete within five days. In his control series, however, involution first occurred on the fifth day. These results led him to conclude that camphor was a causative factor in hastening the involutionary process in the breast.

The indications for interrupting lactation are listed in Table I.

TABLE I. INDICATIONS

INDICATIONS	GROUPS		
	I	IIA	IIB
Prematurity (dead baby)	6	7	6
Unwed mothers	5	0	9
Monstrosities	1	2	2
Tuberculosis	2	1	1
Stillbirths	14	7	10
Cracked nipples	2	5	1
Breast tumor	0	1	0
Cardiac, Grade III	0	1	1
Eclampsia	0	1	0
Pneumonia	0	1	0
Sepsis	0	4	0
Total number of cases	30	30	30

The following procedure advocated by McNeile[4] was adopted:

Two doses of camphor-in-oil, 1½ gr. each, were given intramuscularly (into the buttocks) the first day (in morning and afternoon). One injection of 1½ gr. was then given daily for three successive days, making the total number of injections five. The use of catharties, ice bags, binders, and restriction of fluids were avoided except in the few cases where it was obvious that therapy failed. All breasts were examined every twelve hours for the first forty-eight hours, every six hours for two days and daily thereafter.

For practical purposes, at the start of this investigation it was found necessary to differentiate the reactions in the breasts into the three following degrees:

First degree: The breasts showed absent or slight filling and were symptom-free.

Second degree: Breasts showed moderate fullness accompanied by slight pain and tenderness.

Third degree: Breasts revealed marked fullness (even to the extent of caking) and secretion associated with severe pain and tenderness.

RECORD OF CASES STUDIED

Thirty patients were used as controls (Group I). These patients did not receive injections of camphor-in-oil or catharsis. Neither were fluids restricted. No attempt was made in any way to inhibit lactation. Beginning the third day postpartum in 25 patients, the breasts showed early evidences of lactation (first degree engorgement). Within forty-eight hours, 10 cases showed moderate fullness accompanied by mild pain and tenderness (second degree engorgement), and 15 cases revealed marked engorgement and associated with severe pain and tenderness (third degree engorgement). The acute symptoms lasted approximately thirty-six hours before beginning to subside. By the eighth day, involution was completed (see Fig. 1). In five cases, however, the breasts remained practically symptomless throughout the entire postpartum course. Why the lactating process was inhibited in the five patients cannot be explained, as there was no cause found to be common to all. Therefore, in the control Group I, it is quite evident that the predominant mammary reaction is that of a second degree or third degree engorgement, which begins about the second day postpartum, reaches its height the third or fourth day, lasts for thirty-six hours and then gradually subsides to the nonlactating state about the eighth or ninth day.

Camphor-in-oil was used in 60 postpartum patients (Group II) of whom half received the first injections within twenty-four hours after delivery (Group IIa) and the other half, after the onset of lactation (Group IIb).

The 30 patients in Group IIa who received camphor-in-oil within twenty-four hours after delivery exhibited the following breast reactions (Fig. 2): In 24 patients (80 per cent), either no engorgement or at the most, a first degree reaction developed. In the remaining 6 patients (20 per cent), 2 patients developed a second degree reaction and 4 patients a third degree engorgement, running a course similar to the control series. These patients should be considered as failures. Among the 24 that failed to develop further than a first degree engorgement, there were no factors common to all except for the use of camphor. The age, duration of pregnancy, parity, and indication for weaning were so variable that no relation could be demonstrated between them and the failure of the breasts to progress to further engorgement.

Thirty patients in Group IIb were treated after twenty-four hours postpartum. In 4 patients, all of whom were less than ninety-six hours postpartum, the breasts

exhibited a first degree engorgement before the administration of camphor and in each instance, regression started in six hours and was complete after twenty-four hours. The remaining 26 patients showed either a second degree or a third degree reaction before the injections were started. Those showing the second degree reaction failed to develop a third degree engorgement after the treatment was instituted. Furthermore, regressive changes took place in twelve hours and were complete in forty-eight hours. Approximately the same course occurred in the breasts of those patients who showed a third degree reaction before treatment. After twelve hours, involution began and was complete in less than seventy-two hours (Fig. 3). There was one exception. This patient ran a course similar to the third degree reaction of the control group. The coincidence of breast improvement, following the use of camphor, points to the possibility that the drug exerts in some way an inhibitory influence upon lactation. Here again, the factors of age, duration of pregnancy, parity and indication for weaning were considered as to their possible effect upon involution and were found to be negligible.

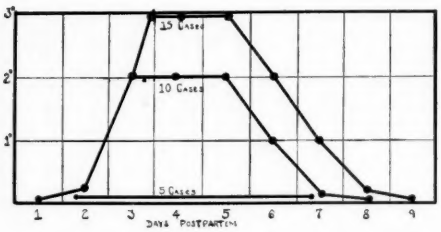

Fig. 1.—Lactation curve, control Group I.

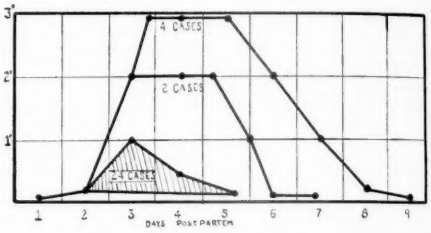

Fig. 2.—Lactation curve, Group IIa.

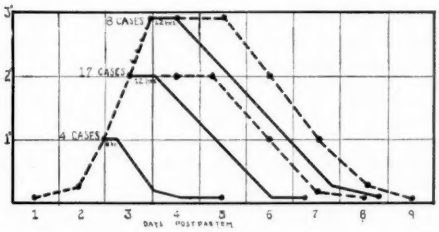

Fig. 3.—Lactation curve, Group IIb. Dotted line respesents lactation curve of control Group I. Solid line represents curve of Group IIb.

In the entire series of 90 cases, there were 12 patients who had a temperature of 100.4° F. or more for forty-eight hours or longer. In only 2 cases could the elevation of temperature be attributed to the engorgement of the breasts. One case was in the control series and the other in a patient in Group IIb, with a third degree engorgement before camphor was instituted. Therefore, camphor-in-oil in this series did not increase the morbidity. It is of interest to note that there were 2 patients in this group who complained of reactions that might be attributed to the use of camphor. One stated that she felt a numbness of both legs, occurring five minutes after the first injection and lasting ten minutes. The other complained of a drawing sensation down both legs lasting half an hour, occurring ten minutes after the first two injections. This patient also claimed that she had a feeling of drowsiness and dizziness following the first injection and lasting one hour. Physical examination failed to reveal findings to explain these symptoms. Whether these local and general reactions were due to camphor-in-oil is difficult to determine.

SUMMARY

Ninety out of 1,000 postpartum cases were studied regarding the effect of camphor-in-oil on the breasts at various periods following delivery. When given within twenty-four hours after delivery, 80 per cent of the patients failed to develop breast engorgement. When given after twenty-four hours and before engorgement developed beyond the first degree stage, inhibition took effect within six hours and the breasts returned to the normal state shortly thereafter.

When the breasts exhibited a second degree reaction before treatment was instituted, the use of camphor-in-oil prevented extension of engorgement to the third degree stage. When camphor-in-oil was given after the breasts reached the second or third degree reaction, the duration of breast engorgement was shortened to twelve hours instead of thirty-six hours. Furthermore, regression to the nonlactating phase was complete within two to three days instead of the usual four to five days. It is therefore evident that the earlier the injections are started, the less the degree and duration of the engorgement, and the quicker the breasts return to their dry state.

Since the writing of this paper, 50 additional patients have been given larger doses of camphor-in-oil (3 gr. twice during first day) with results that seem to be more effective in prevention of lactation.

CONCLUSIONS

1. Intramuscular camphor in oil is an effective method of treatment for relief of breast engorgement.

2. Camphor-in-oil given intramuscularly was found to inhibit lactation.

3. The sooner the injections are started postpartum, the more effective is the action.

4. No marked general or local reactions followed.

5. The advantages of this method over binders, catharsis, sedation and restriction of fluid intake, are that it is more effective, simpler and less disturbing to the patient.

I wish to express my thanks to Dr. Harry Aranow, Director of Obstetrics, and to Dr. Abraham Tamis for his valuable advice and help in planning this paper.

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(1) *Rosenblatt, J.:* Zentralbl. f. Gynäk. **46**: 1523, 1922. (2) *Philpott, N. W.:* Canada Med. J. **20**: 494, 1929. (3) *McNeile, L. G.:* Western J. Surg. Obst. & Gynec. **43**: 61, 1935. (4) *Liegner, B.:* Zentralbl. f. Gynäk. **57**: 244, 1933.

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Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF NOVEMBER 12, 1935

The following papers were presented:

An Unusual Case of Postoperative Embolus. Dr. John J. Madden. (For original article, see page 891.)

Is Superfetation Possible in the Human Being? Dr. William E. Studdiford. (For original article, see page 845.)

MEETING OF DECEMBER 10, 1935

The following papers were presented:

Mild Toxemias of Late Pregnancy. Dr. W. W. Herrick. (For original article, see page 832.)

Intestinal Injuries Following Irradiation for Cancer of the Cervix. Dr. James A. Corscaden.

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 7, 1935

The following paper was presented:

Behavioral Consequences of Cerebral Birth Lesions. Dr. Edgar A. Doll. (For original article, see page 866.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF NOVEMBER 15, 1935

The following papers were presented:

The Influence of Medical Diseases on Obstetric and Fetal Mortality. Dr. Edward Allen and Dr. Carl P. Bauer. (For original article, see page 885.)

Surgical Complications in Pregnancy. Dr. Fred O. Priest. (For original article, see page 878.)

Antepartum Fetal Death. Dr. D. A. Horner.

Positive and Permanent Identification of the Newborn. Dr. Gilbert P. Pond.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Endocrinology

Pende, Nicola: Clinical Classification of Endocrine Diseases, Vestnic Endocrinologii (Moskow) **4:** 355, 1934.

The author suggests the following classification of endocrine diseases in accord with varied syndromes of symptoms: (1) Endocrine temperaments and subendocrinopathic conditions, dependent on hereditary constitution in the majority of cases. (2) Latent and compensated endocrinopathies, representing serious damage of endocrine glands which temporarily does not become actively manifested. Pathologic anatomy and secretory activity do not go parallel. (3) Dissociated, partial and paradoxical endocrinopathies, in which affection of endocrine gland may remain latent or manifests itself in various characteristic symptoms, but at the same time other symptoms may be absent or cause contradictory phenomena. (4) Complete endocrinopathies, i.e., distinctly pronounced afunctional or hypo- and hyperfunctional syndromes. (5) Compound endocrinopathies manifesting themselves in the immediate action of altered endocrine function upon various organs. (6) Associated or pluriglandular endocrinopathies, in which endocrine syndromes are a composite of the syndromes of several affected endocrine glands. (7) Endo-exocrine syndromes as, e.g., in the cases of Mikulicz's disease where a hypertrophy of salivary and lacrimal glands occurs with hypoadrenalism and hypogenitalism. (8) Neuro-endocrinopathic and psycho-endocrinopathic syndromes. On the basis of this category the author dwells upon functional unity of the endocrine apparatus and the neurovegetative system.

ALEXANDER GABRIELIANZ.

Pavlenko, S. M.: The Question of Endocrine Correlation, Vestnic Endocrinologii (Moskow) **4:** 198, 1934.

Not a single existing scheme of the correlation of the endocrine glands has any value because many glands produce several hormones, responsible for varying reactions of the organism. There is no constancy in antagonism and synergism of the glands. Two endocrine glands may be antagonists or synergists depending on the age of the individual; e.g.: Hyperfunction of the thyroid leads to hypofunction of gonads in adults, while in childhood hypofunction of the thyroid causes underdevelopment of the gonads. Furthermore, in adults, hypofunction of the gonads may be due not only to hyperfunction of the thyroid, but to hypofunction as well. The author asserts that many endocrine disturbances are not directly dependent on disturbed function of endocrine glands in regard to quality or quantity of the secreted hormone, but represent pathologic reaction of the peripheral organ in its response to hormonal influence. Only on this basis

can one explain such diseases as partial gigantism, dysthyreosis, Basedow's disease without increase and changes in morphology of the thyroid gland, etc.

ALEXANDER GABRIELIANZ.

Raab, V.: About Fat Regulating Metabolism Substance of the Hypophysis "Lipoitrin," Vestnic Endocrinologii 4: 224, 1934.

Anterior and posterior lobes of the hypophysis contain a substance specifically acting upon fat metabolism (Lipoitrin). It is thermostabile and is destroyed by alkali.

Action of lipoitrin consists in prolonged decrease of the amount of fat in the blood of dogs. In the human, alimentary glycemia disappears after injection of this preparation. The hormone acts upon a center lying in the tuber cinereum.

The physiologic task of lipoitrin, it seems, is controlling those parts of the thermoregulating center which influence caloric utilization of fat.

Hypophyseal and cerebral obesity are explainable as the result of breaking off the neurohormonal mechanisms of utilization of the fat.

ALEXANDER GABRIELIANZ.

Swezy, O.: Some Pitfalls in the Study of Sex Hormones, J. Lab. & Clin. Med. **19**: 561, 1934.

To correlate certain phases of work concerning the interrelations between the gonads and the anterior hypophysis, the author in a review of the literature calls especial attention to some of the pitfalls in the study of sex hormones. These may be enumerated as follows:

The same criteria of the efficacy of administration of sex hormones is fairly general, viz.: The weights of the gonads of immature animals receiving injections for a short period, the opening or closure of the vagina, the tests in many cases being repeated in the same animals. It has been shown that the ovary has no necessary relation to the vagina upon experimental hormonal injection and further that these vaginal changes may occur with no corresponding changes in either uterus or ovary. The vaginal smear method is, therefore, an unsuitable one for sole reliance as an assay test for sex hormones, and it accounts for many of the variable results reported. Likewise, the practice of using the same animals repeatedly at frequent intervals without rest periods may produce variable results.

The use of the weight of the ovary as an assay test is likewise no infallible guide to the kind of change induced by hormone treatment. A considerable amount of follicular growth may be found without a significant increase in the weight of the ovary. The relation of estrin or the factor inducing cornification in the vagina of rodents to folliculin or factor inducing growth in the endometrium is fraught with confusion. Under experimental conditions it seems that the factor inducing cornification is not identical with that inducing growth in the uterus. Their assumed identity has resulted in the widespread use of the vaginal smear test as the important one in the assay of these hormones. Some believe a single hormone may be responsible for the changes in the uterus and vagina, the relation being a quantitative one; others that two factors are involved. Cornification has no recognized place in the human cycle and, therefore, a clarification of these relations and the hormones associated with them can be obtained only by more critical analyses of the experiments conducted with them.

In all experimental work on normal animals, the hypophysis of the test animal largely decides the results when sex hormones are being studied. This is probably due to an activator in some preparations, including human pregnancy ex-

tracts and the hypophysis of the infantile rat, which is able to stimulate the hypophysis of the host to increased hormone production. The difficulties of determining the hormone content of any preparation are thus increased, since this can be done accurately only when the animal's own hypophysis is removed.

W. B. SERBIN.

Young, A. M.: Observations on the Technic of the Friedman Test for Pregnancy, J. Lab. & Clin. Med. **19:** 1224, 1934.

In a series of 350 Friedman tests for pregnancy, Young obtained the following results: 92 true positives in uterine pregnancy; 2 positives in intact ectopic pregnancy, and 1 in hydatid mole. There was one false positive. There were 131 true negatives in which 69 had no pelvic pathology and 79 had various types of pelvic disease. One male urine was used which gave a negative test; there were five doubtful early tests. There was one false negative and 114 tests were experimental. The earliest positive test in the series was thirty-two days after the last menstrual period.

The author recommends the following procedures in carrying out the Friedman test: Selection of ordinary mature domestic female rabbits weighing from 2 to 4 kg.; isolation of animals in individual cages; use of morphine sulphate gr. ½ to gr. 2 intravenously as an anesthetic; preliminary laparotomy and inspection of ovaries with selection of animals with ripe or nearly ripe follicles but no corpora hemorrhagica or corpora lutea; intravenous injection of 15 c.c. of clear, filtered, first morning specimen of urine, warmed to body temperature, sp. gr. of 1.015 or higher, the dose repeated in about four hours. Forty-eight hours after the first injection the wound is opened and the ovaries are reinspected. If ovaries are grossly positive, one ovary is removed and examined microscopically by frozen section. The presence of lutein tissue in the wall of one or more follicles associated with some hemorrhage into the follicle constitutes an undoubtedly positive reaction. If the ovaries have no corpora hemorrhagica the wound is closed and the rabbit injected with 15 c.c. of known positive urine or concentrated urine and forty-eight hours after the injection of the positive control urine the wound is opened and the ovaries are reinspected. If the ovaries now contain corpora hemorrhagica and lutein tissue, the final report of a negative test with the urine for diagnosis is given. If facilities are not available for making frozen sections, a reinspection of the ovaries on the fifth or sixth day after injection will show sufficient lutein tissue grossly to make a positive diagnosis.

W. B. SERBIN.

Pratt, J. P.: The Human Corpus Luteum and Progestin, Endocrinology **18:** 667, 1934.

Two hormones have been extracted from the corpus luteum of animals, the estrogenic substance and progestin. The presence of progestin, first extracted from the corpus luteum of the sow, has not been demonstrated in many species.

The author investigated its presence in corpora lutea removed at operation. A total of 131.5 gm. was thus obtained and the Corner-Allen method of extraction used. The assay of the human material was paralleled by similar product from the sow. In the sow, tests for progestin are positive in 20 ± 5 gm. of material. The human material gave negative results up to 40 gm. These experiments indicate that progestin is not as plentiful in human as in hog corpora lutea or that its presence is confined to certain periods in the menstrual cycle not yet determined.

J. THORNWELL WITHERSPOON.

Wodon, J. L.: The Menopause and the Biological Diagnosis of Pregnancy, Rev. franç. de gynéc. et d'obst. **29:** 927, 1934.

During the menopause, whether spontaneous or artificially produced, one sometimes finds in the urine a substance which is capable of producing follicular hemorrhages in the rabbit, in spite of the absence of pregnancy. Under such conditions the Aschheim-Zondek test presents the same possibility of error as the Friedman test. Since the substance which is responsible for the follicular hemorrhages is weaker than it is during normal pregnancy, an error in biologic diagnosis may be avoided by simultaneously injecting two animals, one with 15 c.c. and the other with 5 c.c. of urine. A diagnosis of pregnancy should not be made unless both rabbits show a positive reaction.

J. P. GREENHILL.

Pratt, J. P.: The Human Corpus Luteum, Arch. Path. **19:** 380 and 545, 1935.

Pratt reviews the recorded studies of the human corpus luteum. He considers first its history, origin, macroscopic and microscopic structure, maturation, physiology, chemistry, and pathology. His comments are as follows: The literature on corpus luteum is voluminous with often no distinction made to indicate the species studied. It is difficult, therefore, to separate references to human beings from those of lower animals. In many instances no distinction is made between estrus and menstruation. However, animal experimentation has laid the foundation for interpretation of human problems. There is quite general agreement as to the anatomic structure of the corpus luteum but the concept of its function is still in transition. Accumulated knowledge of the past has been of value but the recent progress in chemistry epitomized by the isolation of theelin in pure crystalline form from many sources including the corpus luteum and the isolation of progestin from corpora lutea of some animals, marks the beginning of a new era.

The discovery of the control of ovarian function by the anterior lobe of the hypophysis is important but it is unwise to predict that all disturbed functions of the gonads can be regulated by the administration of incretions of the anterior lobe. The physiologic function intrinsic within the gonads must account for some of the major phenomena of the reproductive cycle. With these new developments it is possible to hope that eventually a rational therapy will be developed. Many therapeutic ventures to prevent disturbances of nidation have been based on the assumption that the corpus luteum is essential to nidation. Until more evidence is adduced to show that a specific hormone is provided by the corpus luteum which influences nidation, such therapy must be classed as empirical. Interpretation should be critical so that progress may continue.

W. B. SERBIN.

Fluhmann, C. F.: A New Procedure for the Demonstration of Estrin in the Blood of Women, Endocrinology **18:** 705, 1934.

Fluhmann describes a biologic test for the demonstration of estrin in the blood of women. The test depends on the injection of small amounts of untreated serums into spayed mice. A positive result is indicated by the production of a "mucification" of the vaginal mucosa. The method may be applied to quantitative studies, provided a sufficient number of test animals are employed.

The examination of 80 specimens of blood obtained from 46 women at different stages of their menstrual cycles showed that the maximal concentration of estrin

was reached during the middle of the interval phase, a secondary rise occurred at the time of the flow, and it was diminished just before and after menstruation.

J. THORNWELL WITHERSPOON.

Ferringo, P.: Estrogen Elimination in Women With a Normal Sexual Cycle and in Women Affected by Amenorrhea, Clin. ostet. **37:** 129, 1935.

The maximum elimination of 300 rat units per 1,000 c.c. of urine was found in a woman with a normal sexual cycle. The moderate elimination of 170 rat units per 1,000 c.c. of urine in twenty-four hours occurred in a woman during the menopause. The minimum elimination of 100 rat units per 1,000 c.c. of urine in thirty-six hours was observed in a woman with amenorrhea.

AUGUST F. DARO.

Marx, Rudolph: Influence of Hysterectomy on Endocrine Balance, Am. J. Surg. **28:** 117, 1935.

Suggested by the hypothesis of Sessums and Murphy, that ovarian conservation after hysterectomy delays the onset of the menopause and diminishes its unpleasant symptoms, the author offers additional observations indicating that the uterus is not only an organ of reproduction but that it plays an important part in the regulation of the endocrine balance during the period of sexual maturity. He suggests that the ovarian-uterine hormonal reaction is not altogether one-sided, from ovary to uterus, but that the endometrium also secretes a hormone which acts upon the ovary. Hence, the ideal clinical relation after hysterectomy is to conserve sufficient endometrium, with one or both ovaries, to preserve this ovarian-uterine hormonal balance.

J. THORNWELL WITHERSPOON.

Ellison, E. T., and Wolfe, J. M.: The Effect of Castration on the Anterior Hypophysis of the Female Rat, Endocrinology **18:** 555, 1934.

Studies were made on the pituitaries of 100 female rats from which the ovaries had been removed at various intervals (5-500 days) before they were sacrificed. It appeared that there is a quantitative increase in the percentage of basophile cells until about the thirtieth day of castration. After this period there is a gradual decrease of these elements. There is a moderate increase in the percentage of eosinophile cells during the first sixty days of castration. Later they tend to decrease in number. There is no morphologic change in the chromophobe type of cell after castration.

J. THORNWELL WITHERSPOON.

Damm, P.: Quantitative Examinations of Hormones in the Urine, Acta obst. et gynec. Scandinav. **14:** 129, 1934.

Observations were carried out in regard to the amount of prolan A in the urine of operatively castrated women at short intervals after the operation. At the same time the urine was examined with regard to the amount of folliculin contained in it, mostly with negative result. The amounts dealt with in the quantitative determination of prolan A were so small that it was necessary to use the precipitation method. Prolan A was already present about two weeks after castration. The hormonal examination was also carried out during folliculin treatment, which did not seem to influence the secretion of Prolan A. This result, however, may be due to the small amount of folliculin given. The amount of folliculin secreted during the treatment shows a considerable deficiency, probably

because most of the folliculin is retained in the organism in one form or another. During the treatment the subjective symptoms disappear, which seems to indicate that these symptoms are due to a lack of folliculin, and not to an increased secretion of prolan A. The investigations confirm the importance of an hormonal analysis in patients who have been subjected to a partial removal of the adnexa, as by this means it is possible to assure oneself of the functional ability of the remaining ovarian tissue. This is of great importance for a decision on the necessity of a later hormonal substitution therapy.

J. P. GREENHILL.

Lassen, H. C. A., and Brandstrup, E.: Serial Studies on Occurrence of Prolan A and B in Urine of Women Castrated by X-ray Treatment or by Operation, Acta obst. et gynec. Scandinav. **14**: 89, 1934.

In 36 cases of x-ray castration and in 10 cases of operative castration, a total of 436 tests for prolan in the urine were made about once a month for from three to thirty-one months after castration. With the technic employed in these tests, prolan could be demonstrated only when present in amounts above 400 M.U. per liter of urine.

The prolan A reaction was positive in about 30 per cent of all the urine specimens (343) examined after the irradiation; the prolan B reaction was positive in 7 per cent. The frequency of the prolan A reaction was almost the same throughout the observation period; the prolan B reaction was most frequent (11 to 12 per cent) during the first half year after castration.

Positive prolan A reaction was found in about half of the urine specimens (93) examined after operation; prolan B reaction in 9 per cent. The prolan reactions are most frequent during the first six months after operation. All 10 patients excreted, at some time or other after operation, prolan A in amounts above 400 M.U. per liter of urine, most of them within the first half year after operation. Six patients gave positive prolan B reaction within the same period.

In the 35 cases in which both the prolan A and B reactions were positive, HVR.-II was positive in 24. In control material suitable for comparison, tests with the technic employed gave prolan A reaction in 15 per cent of the cases and prolan B reaction 1 to 2 per cent. Sixty-three patients in the climacteric age showed, with one test in each case, prolan B reaction in 14 per cent of the cases.

J. P. GREENHILL.

Nelson, W. O.: Concerning the Anterior Pituitary-Gonadal Interrelations, Endocrinology **19**: 187, 1935.

Cell counts on the anterior lobes from 68 normal male and 56 normal female rats have shown that the male gland has a higher percentage of basophiles and acidophiles and a lower percentage of chromophobes than that of the female. The anterior pituitaries from 25 castrate male and 17 spayed female rats which had been injected with estrin showed a profound decrease in the percentage of both castration cells and nonvacuolated basophiles.

That the suppressing influence of the gonads on the gonadotropic activity of the hypophysis appears to be conducted through the action of the gonad hormones, particularly estrin, on the secretory cycle of the anterior lobe basophiles has been suggested. On the basis of the above physiologic and histologic evidence indicating a fundamental difference in the sensitivity to gonad hormone on the part of the male and female hypophysis, an explanation is offered for the cyclic character of female reproduction and the absence of a cycle in the male. In the female the production of estrogenic hormone decreases with lack of stimulation, the gonado-

tropic hormone is secreted again and a new cycle is initiated. In the male the hypophysis is less easily influenced by gonad hormone with the result that apparently it is never suppressed to the extent that the male reproductive functions exhibit cyclic characteristics.

J. THORNWELL WITHERSPOON.

Zondek, B.: Primary Polyhormonal Amenorrhea With Glandular Cystic Hyperplastic Endometrium, Acta obst. et gynec. Scandinav. **13:** 309, 1934.

Zondek's earlier investigations showed that both amenorrhea and hemorrhage may be the result of the same functional process, namely, a too strong and protracted production of follicle hormones (folliculin). Those observations led him to the idea of polyhormonal pathologic syndromes. In the chain of proof there was still a link missing, however. It had not yet been proved that the mucosa of the uterus showed the same changes in the case of amenorrhea as in the case of hemorrhage. Zondek now describes a case of primary polyhormonal amenorrhea with persisting follicle, highly increased secretion of folliculin, and glandular-cystic-hyperplastic uterine mucosa. Hence the same anatomic change can be found in the case of amenorrhea as in the case of polyhormonal hemorrhage (metropathia hemorrhagica).

J. P. GREENHILL.

McClellan, G. S., Phelps, Doris, and Burch, J. C.: Endometrial Studies, Endocrinology **19:** 321, 1935.

Three series of experiments dealing with the interpretation of human endometrial change in terms of ovarian activity are reported. These include histologic studies of the normally menstruating and the bleeding hyperplastic endometrium; the relation of endometrial growth, blood and urine estrin and bleeding periods in a case of endometrial hyperplasia; and the effect exerted on the endometrium of a castrated woman by injections of estrogenic and corpus luteum hormones. Specimens of endometrium in all cases were obtained by the punch biopsy method.

The histologic characteristics of 35 specimens of normally menstruating endometrium were compared with those of 25 typical specimens of bleeding hyperplastic endometrium. The former is characterized by progestational changes, evidence of degeneration with no evidence of active, vigorous growth, and by relatively little hemorrhage and no edema. The tissue consists chiefly of the basal layer. The bleeding hyperplastic endometrium is characterized by every evidence of vigorous growth and by considerable hemorrhage and edema. It shows no progestational changes, and the tissue is chiefly from the upper layers.

In a case of endometrial hyperplasia, weekly biopsies were obtained over a period of two months. Specimens of blood and urine, taken on the days biopsies were obtained, were assayed for estrin content. The so-called "Swiss-cheese" pattern was found in specimens taken near the beginning of the observation period but was not found in later specimens. In the interval between bleeding periods and near the onset of the latter, the greatest evidence of endometrial growth was found. The level of blood estrin was highest during these intervals and showed a decline before the onset of the succeeding period of bleeding.

A castrated woman, aged forty years, was given a series of injections of estrogenic and corpus luteum hormones over a period of one month. A total of 5 intramuscular injections of 50,000 M.U. each, administered twice weekly, of estrogenic hormone was followed by 5 daily injections of 10 rabbit units each of corpus luteum hormone. Administration of the latter was begun 4 days after the last injection of estrogenic hormone. Weekly biopsies were taken throughout the experiment. The estrogenic hormone provoked a mild growth of the endometrium.

Bleeding began four days after the last injection of this hormone and continued for ten days. A slight progestational reaction appeared during the period of injection of the corpus luteum hormone.

Punch biopsy is a safe and reliable method of obtaining endometrium for clinical and research purposes, and offers a means of differentiating luteal from aluteal bleeding.

"Swiss-cheese" pattern is not a constant accompaniment of endometrial hyperplasia and the diagnosis of this condition can and should be made in its absence.

J. THORNWELL WITHERSPOON.

Selye, H., Collip, J. B., and Thomson, D. L.: Endocrine Interrelations During Pregnancy, Endocrinology **19**: 151, 1935.

In the rat, ovariectomy during gestation was found not to interfere with the life of the placenta. It terminates pregnancy only because it causes death of the fetus; and the dead fetus, if it is large enough at the time of the intervention, will cause the abortion of the whole gestation sac, simply acting as a foreign body. The probable cause of death of the fetus is the partial involution of the uterus which considerably increases the pressure in the gestation sac.

The placenta of the rat must produce the corpus luteum hormone, since the uterus was found to show distinct progestational changes, and the mammary gland to be maintained in a well-developed condition for as long as six days after the simultaneous removal of the ovaries and all the embryos.

The placenta survived in apparent functional integrity after removal of the ovaries and the fetuses, hence it is independent of ovarian hormones even in the rat, a species in which ovariectomy invariably terminates gestation. Since the life-span of the placenta was not markedly influenced by the removal of the embryos, the length of the gestation period must be determined by factors inherent in the placenta.

J. THORNWELL WITHERSPOON.

Rosenblat, J., and Nathan, F.: Modifications of the Ovaries of Pregnant Women and Pregnant Rabbits as an Expression of an Aschheim-Zondek Autoreaction, Rev. franç. de gynéc. et d'obst. **29**: 104, 1934.

There is very little in the literature concerning the changes in the ovaries of pregnant women. Since 1931 the authors have had occasion to examine the ovaries of 10 women during operation for extrauterine pregnancy. Only healthy ovaries were studied. In every single case the authors found an increase in size of the ovary, a distinct extravasation in the graafian follicles, hence reactions which are characteristic of the Aschheim-Zondek test for pregnancy. Since microscopic control of these cases could not be undertaken, the authors performed experiments on animals. They found among pregnant rabbits the same changes which they observed in mice and immature rabbits after the injection of urine obtained from pregnant women. The authors conclude that the action of hormones which circulate in the blood of pregnant women and of pregnant rabbits is much more extensive that heretofore known.

J. P. GREENHILL.

Anker, H., and Laland, P.: Investigation of Prolan in Emesis and Hyperemesis Gravidarum, Acta obst. et gynec. Scandinav. **14**: 310, 1934.

The authors investigated the urine, blood serum, and gastric contents of five patients with hyperemesis and ordinary vomiting of pregnancy. In two they found subnormal prolan contents in the urine. In five they found an excessive prolan

content in the blood and in two an inconstant prolan secretion in the vomitus. At the time the vomiting ceased there was a rise in the prolan content of the urine in three cases and a fall in the prolan content of the blood serum in two. In control cases the urine and blood serum of pregnant women showed normal prolan contents.

J. P. GREENHILL.

Dworzack and Poleschka: The Hormonal Functions of Granulosa Cell Tumors, Arch. f. Gynäk. **154:** 441, 1933.

Hypertrophy of the endometrium and myometrium together with metrorrhagia and breast hypertrophy are frequently found with granulosa cell tumors. The endometrial change is usually a glandular cystic hyperplasia and is practically always present. Occasionally a decidua-like change is found. Such changes must be due to hormonal activity of these tumors. The authors were unable to find any definite anterior hypophysis reaction but found that the elimination of the follicular hormone jumped from 2 to 3 units per liter of urine during the intermenstrual period of 50 units per liter when granulosa cell tumors were present. Such a hyperhormonal state produces the uterine enlargement and the endometrial hyperplasia. The corpus luteum hormone is also probably produced, since there is occasionally a decidua formation.

The authors believe that it will soon be possible to diagnose granulosa cell tumors before operation. They believe that frozen sections should be made whenever this type of tumor is suspected or diagnosed during operation, in order that a radical operation may be performed if this type of tumor is diagnosed. The question of recurrences following operation and postoperative irradiation can be determined by examinations for the hormones produced by the tumor.

RALPH A. REIS.

Bergstrand, H.: The Nature of Virilizing Ovarian Tumors, Acta obst. et gynec. Scandinav. **13:** 336, 1934.

The author describes ovarian tumors in 4 cases of hirsutism from his own series and he also microscopically examined the two cases reported by Berner and Strassmann. In two of his own cases he proved the growth to be a folliculoma or a granulosa cell tumor, especially as the strands of tumor cells form bodies resembling atretic follicles. On the basis of these two cases, he made a histologic analysis of the four others, and came to the conclusion that they are fundamentally of the same nature. In one of them, he found an unmistakable ovum in the center of the large mass of malignant tumor tissue. Besides ovarian elements, granulosa and lutein cells, cysts lined with columnar epithelium and containing mucus occurred in 3 cases. In 2 cases these cysts were quite distinct from the ovarian elements of the tumor. He therefore considers these tumors to be a combined malformation of the germinal epithelium of the mesonephros and of Wolff's duct or Mueller's duct. From the clinical point of view it is interesting to note that these tumors, which microscopically are shaped like ovaries, often show mitosis and other signs of rapid growth, but nevertheless are as a rule clinically benign if removed in time. In one of the author's cases, however, the patient died from extensive metastases of the peritoneum.

The microscopic examination gives no clue whether the active hormone is produced by the granulosa or the lutein cells of the tumor. The investigations of Steinach and Kun, who in 1931 were able to demonstrate the virilizing effect on guinea pigs of corpus luteum extract, seem to indicate that this secretion is a function of the lutein cells.

The author's researches have led him to reject all earlier theories ascribing hirsutism to the internal secretion of tumors arising in a hypothetical testicular component of the embryonic ovary.

J. P. GREENHILL.

Novak, E.: The Endocrine Effects of Certain Ovarian Tumors, Am. J. M. Sc. **187:** 599, 1934.

Certain tumors of the ovary are capable of highly developed endocrine function. The two most clearly defined types are the granulosa cell tumors, and the so-called arrhenoblastomata. The granulosa cell tumors exert a feminizing effect, through the production of theelin by the tumor cells, so that in older women, even beyond the menopause, they produce most often a hyperplasia of the endometrium, associated with periodic bleeding and increased size of the uterus. In the few cases seen in very young children, they have produced the syndrome of precocious puberty.

The arrhenoblastomata, on the other hand, have a definitely masculinizing tendency, as might be expected from the fact that they apparently have their origin from undifferentiated epithelium in the region of the rete ovarii. Under conditions which are not clear these cells, capable of developing along either male or female lines, may assume definitely masculine tendencies, such as amenorrhea, breast atrophy, masculine hair distribution, deepening of the voice, and hypertrophy of the clitoris. Removal of the tumor brings about a regression of these symptoms.

J. THORNWELL WITHERSPOON.

Brindeau, Riehl; Hinglais, H., and Hinglais, M.: The Presence of a Large Amount of Luteinizing Hormone in the Urine in a Case of Lutein Cyst, Bull. Soc. d'obst. et de gynéc. **24:** 38, 1935.

The authors observed a second case of lutein cyst associated with secretion of prolans A and B. The amount of hormone present could lead one to suspect a pregnancy, but quantitative methods eliminated the diagnosis of pregnancy. The amount of prolan B in the urine of the present case (120 units per liter) is the largest the authors have ever recovered outside of pregnancy or a chorionepithelioma. They have never obtained more than 100 units from a nonpregnant individual. They therefore believe it best to fix the upper limit at 150 units in order to eliminate any errors in the diagnosis of pregnancy. The hormone disappeared rapidly from the urine after the removal of the cyst.

J. P. GREENHILL.

Murphy, Douglas P.: The Excretion of Ovary Stimulating Hormone in the Urine During Pregnancy, Surg. Gynec. Obst. **56:** 914, 1933.

The amount of ovary-stimulating hormone (expressed in rabbit units) in 30 twenty-four-hour specimens of urine of 24 pregnant women is recorded. Some patients were normal, others exhibited mild complications of pregnancy, the majority were in the last third of gestation when their urine was collected.

The amount of hormone excreted in twenty-four hours varied from less than 100 to more than 12,000 rabbit units; the majority of patients voided less than 2,000 rabbit units.

The excretion of hormone by the same individual from day to day was relatively constant and was independent of the output of urine.

From these observations, it is concluded that: (1) Variation in the output of urine has no significant influence upon the amount of ovary-stimulating hormone

which is excreted. (2) Estimation of the rate of excretion of ovary-stimulating hormone should be based upon measurement of the hormone in the urine that is passed in a twenty-four-hour period, and not upon the amount in a smaller sample of urine.

WILLIAM C. HENSKE.

Books Received

POST-GRADUATE SURGERY. Edited by Rodney Maingot, Senior Surgeon of the Royal Waterloo Hospital and Southend General Hospital. Volume I, with 846 figures in the text, 1,742 pages. D. Appleton-Century Company, New York, 1936.

CLINIQUES OBSTÉTRICALES, par L. Devraigne, chargé de cours de clinique annexe de la faculté de médecine de Paris. 240 pages. G. Doin & Cie, editeurs, Paris, 1936.

ANNUAL REPORT for the year 1933 of the Minneapolis General Hospital. Published in 3 parts.

CHILD PSYCHIATRY. By Leo Kanner, M. D., Associate Professor of Psychiatry, Johns Hopkins University. Pp. 527. Published by Charles C. Thomas, Springfield, Ill., 1935.

PEDIATRIC NURSING. By John Zahorsky, M.D., Professor of Pediatrics and Director of Department of Pediatrics, St. Louis University School of Medicine, etc. With 144 illustrations in the text and 7 color plates, 568 pages. The C. V. Mosby Co., St. Louis, 1936.

AN INDEX OF DIFFERENTIAL DIAGNOSIS OF MANY SYMPTOMS. By various authors, edited by Herbert French, Consulting Physician to Guy's Hospital. Fifth edition, with 742 illustrations of which 196 are colored, with 1145 pages. William Wood & Co., Baltimore, 1936.

LA SINFISIOTOMIA EN ESPAÑA. Por Dr. Angel Guerrero Abellan, Barcelona, 1936.

ABORTION, SPONTANEOUS AND INDUCED. Medical and Social Aspects. By Frederick J. Taussig, M.D., Professor of Clinical Obstetrics and Gynecology, Washington University School of Medicine. 536 pages. Illustrated. The C. V. Mosby Co., St. Louis, 1936.

A TEXTBOOK OF OBSTETRICS. For Students and Practitioners. By Frederick C. Irving, M.D., Professor of Obstetrics, Harvard Medical School; Visiting Obstetrician, Boston Lying-In Hospital. 558 pages. The Macmillan Company, New York, 1936.

LEHRBUCH DER GEBURTSHILFE. Von Dr. Rud. Th. v. Jaschke. Vierte Auflage, mit 573 zum Teile farbigen Abbildungen. 770 Seiten. Verlag von Julius Springer, Berlin, 1935.

MEDICAL PAPERS. Dedicated to Henry Asbury Christian, physician and teacher, from his present and past associates and house officers at the Peter Bent Brigham Hospital, Boston, Mass. In honor of his sixtieth birthday, Feb. 17, 1936.

THE SINGLE WOMAN AND HER EMOTIONAL PROBLEMS. By Laura Hutton, Physician, Institute of Medical Psychology, London. William Wood and Co., Baltimore, 1935.

PSYCHOLOGY OF SEX. A Manual for Students. By Havelock Ellis. 377 pages. Emerson Books, Inc., New York, 1935.

THE TRUE PHYSICIAN. The Modern Doctor of the Old School. By Wingate M. Johnson, M.D. 157 pages. The Macmillan Co., New York, 1936.

THE BALANCED DIET. By Logan Clendening, M.D. Professor of Clinical Medicine, University of Kansas. Illustrated. 207 pages. D. Appleton-Century Co., New York, 1936.

Item

American Board of Obstetrics and Gynecology

The annual informal dinner and general conference of Diplomates of the American Board of Obstetrics and Gynecology attending the American Medical Convention will be held at the Hotel Kansas Citian, Kansas City, Missouri, on Wednesday, May 13, 1936, at 7:00 P.M.

At this dinner the successful candidates of the two preceding days' examinations will be presented in person, and short addresses will be made by two guest speakers and several members of the Board.

Diplomates of the Board and physicians interested in obstetrics and gynecology are invited to attend. Tickets ($2.00 each) may be obtained from Dr. Joseph L. Baer, 104 S. Michigan Ave., Chicago, or at the door.